UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-Q

(Mark One)

☒ **QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934.**

For the quarterly period ended June 30, 2016

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934.**

For the transition period from _____ to _____.

Commission File No. 001-36276

ULTRAGENYX PHARMACEUTICAL INC.

(Exact name of registrant as specified in its charter)

Delaware	**27-2546083**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
60 Leveroni Court **Novato, California**	**94949**
(Address of principal executive offices)	*(Zip Code)*

(415) 483-8800
(Registrant's telephone number, including area code)

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities and Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. YES **R** NO ☐

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Website, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). YES **R** NO ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer	**R**	Accelerated filer	☐
Non-accelerated filer	☐ (Do not check if a smaller reporting company)	Smaller reporting company	☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). YES ☐ NO **R**

As of August 3, 2016, the registrant had 39,435,593 shares of common stock issued and outstanding.

ULTRAGENYX PHARMACEUTICAL INC.

FORM 10-Q FOR THE QUARTER ENDED JUNE 30, 2016

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q contains forward-looking statements that involve risks and uncertainties. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. All statements other than statements of historical facts contained in this Quarterly Report on Form 10-Q are forward-looking statements. In some cases, you can identify forward-looking statements by words such as “anticipate,” “believe,” “contemplate,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “seek,” “should,” “target,” “will,” “would,” or the negative of these words, or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- our expectations regarding the timing of commencing our clinical studies and reporting results from same;
- the timing and likelihood of regulatory approvals for our product candidates;
- the potential market opportunities for commercializing our product candidates;
- our expectations regarding the potential market size and the size of the patient populations for our product candidates, if approved for commercial use;
- estimates of our expenses, future revenue, capital requirements, and our needs for additional financing;
- our ability to develop, acquire, and advance product candidates into, and successfully complete, clinical studies;
- the implementation of our business model and strategic plans for our business and product candidates;
- the initiation, timing, progress, and results of future preclinical studies and clinical studies, and our research and development programs;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates;
- our ability to maintain and establish collaborations or obtain additional funding;
- our ability to maintain and establish relationships with third parties, such as contract research organizations, suppliers, and distributors;
- our financial performance and the expansion of our organization;
- our ability to obtain supply of our product candidates;
- developments and projections relating to our competitors and our industry; and
- other risks and uncertainties, including those listed under Part II, Item 1A. Risk Factors.

Any forward-looking statements in this Quarterly Report on Form 10-Q reflect our current views with respect to future events or to our future financial performance and involve known and unknown risks, uncertainties, and other factors that may cause our actual results, performance, or achievements to be materially different from any future results, performance, or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those discussed under Part II, Item 1A. Risk Factors and discussed elsewhere in this Quarterly Report on Form 10-Q. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

This Quarterly Report on Form 10-Q also contains estimates, projections, and other information concerning our industry, our business, and the markets for certain diseases, including data regarding the estimated size of those markets, and the incidence and prevalence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research, or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market, and other data from reports, research surveys, studies, and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data, and similar sources.

PART I. FINANCIAL INFORMATION

Item 1. ***Financial Statements***

ULTRAGENYX PHARMACEUTICAL INC.
CONDENSED CONSOLIDATED BALANCE SHEETS
(Unaudited)
(In thousands, except share and per share amounts)

	June 30, 2016	December 31, 2015
Assets		
Current assets:		
Cash and cash equivalents	$ 55,069	$ 93,569
Short-term investments	336,734	343,428
Restricted cash	1,482	150
Prepaid expenses and other current assets	17,799	13,060
Total current assets	411,084	450,207
Property and equipment, net	17,054	7,373
Restricted cash	2,346	2,135
Long-term investments	50,021	99,259
Other assets	1,446	595
Total assets	$ 481,951	$ 559,569
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 6,954	$ 2,942
Accrued liabilities	24,714	24,784
Deferred rent—current portion	315	192
Total current liabilities	31,983	27,918
Other liabilities	6,073	561
Total liabilities	38,056	28,479
Stockholders' equity:		
Preferred stock — 25,000,000 shares authorized; nil outstanding as of June 30, 2016 and December 31, 2015	—	—
Common stock — 250,000,000 shares authorized; 39,046,247 and 38,882,394 shares issued and outstanding as of June 30, 2016 and December 31, 2015, respectively	39	39
Additional paid-in capital	837,943	816,578
Accumulated other comprehensive income (loss)	252	(868)
Accumulated deficit	(394,339)	(284,659)
Total stockholders' equity	443,895	531,090
Total liabilities and stockholders' equity	$ 481,951	$ 559,569

See accompanying notes.

ULTRAGENYX PHARMACEUTICAL INC.
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS
(Unaudited)
(In thousands, except share and per share amounts)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2016	2015	2016	2015
Revenue	$ 17	$ -	$ 17	$ -
Operating expenses:				
Research and development	43,332	23,104	83,747	40,468
General and administrative	14,738	7,038	27,945	11,176
Total operating expenses	58,070	30,142	111,692	51,644
Loss from operations	(58,053)	(30,142)	(111,675)	(51,644)
Other income (expense), net:				
Interest income	971	456	1,955	729
Other income (expense), net	159	(101)	40	(251)
Total other income (expense), net	1,130	355	1,995	478
Net loss	$ (56,923)	$ (29,787)	$ (109,680)	$ (51,166)
Net loss per share, basic and diluted	$ (1.46)	$ (0.83)	$ (2.81)	$ (1.46)
Shares used in computing net loss per share, basic and diluted	39,028,701	35,937,442	38,999,439	34,997,498

See accompanying notes.

ULTRAGENYX PHARMACEUTICAL INC.
CONDENSED CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS
(Unaudited)
(In thousands)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2016	2015	2016	2015
Net loss	$ (56,923)	$ (29,787)	$ (109,680)	$ (51,166)
Other comprehensive income:				
Foreign currency translation adjustments	11	-	11	-
Unrealized gain (loss) on available-for-sale securities	149	(115)	1,109	(35)
Other comprehensive income (loss):	160	(115)	1,120	(35)
Total comprehensive loss	$ (56,763)	$ (29,902)	$ (108,560)	$ (51,201)

See accompanying notes.

ULTRAGENYX PHARMACEUTICAL INC.
CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS
(Unaudited)
(In thousands)

	Six Months Ended June 30,	
	2016	**2015**
Operating activities:		
Net loss	$ (109,680)	$ (51,166)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	1,236	463
Amortization of premium (discount) on investment securities, net	3,215	2,233
Stock-based compensation	21,077	7,499
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(4,554)	(3,501)
Other assets	(851)	(16)
Accounts payable	2,825	4,777
Accrued liabilities and other liabilities	2,182	4,779
Net cash used in operating activities	(84,550)	(34,932)
Investing activities:		
Purchase of property and equipment	(6,521)	(1,054)
Purchase of investments	(223,123)	(242,404)
Proceeds from the sale of investments	54,332	20,263
Proceeds from maturities of investments	222,616	109,358
Increase in restricted cash	(1,543)	(1,239)
Net cash provided by (used in) investing activities	45,761	(115,076)
Financing activities:		
Proceeds from issuance of common stock, net	289	178,035
Net cash provided by financing activities	289	178,035
Net increase (decrease) in cash and cash equivalents	(38,500)	28,027
Cash and cash equivalents at beginning of period	93,569	24,324
Cash and cash equivalents at end of period	$ 55,069	$ 52,351

See accompanying notes.

1. Organization

Ultragenyx Pharmaceutical Inc. (the Company) is a biopharmaceutical company and was incorporated in California on April 22, 2010. The Company subsequently reincorporated in the state of Delaware in June 2011.

The Company is focused on the identification, acquisition, development, and commercialization of novel products for the treatment of rare and ultra-rare diseases, with a focus on serious, debilitating genetic diseases. The Company is currently conducting a Phase 3 study of aceneuramic acid extended-release (Ace-ER) in patients with GNE myopathy, which is also known as hereditary inclusion body myopathy, a progressive muscle-wasting disorder; a Phase 3 study of recombinant human beta-glucuronidase (rhGUS) in patients with mucopolysaccharidosis 7 (MPS 7), a rare lysosomal storage disease; a Phase 2 clinical study for UX007 in patients with glucose transporter type-1 deficiency syndrome (Glut1 DS), a brain energy deficiency; a Phase 2 clinical study of UX007 in patients severely affected by long-chain fatty acid oxidation disorders (LC-FAOD), a genetic disorder in which the body is unable to convert long chain fatty acids into energy; and Phase 2 and Phase 3 studies of KRN23, an antibody targeting fibroblast growth factor 23, or FGF23, in patients with X-linked hypophosphatemia (XLH) and tumor-induced osteomalacia (TIO), both rare diseases that impair bone mineralization. The Company operates as one reportable segment.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying unaudited condensed consolidated financial statements include the amounts of the Company and our wholly-owned subsidiaries and have been prepared in accordance with U.S. generally accepted accounting principles (GAAP) for interim financial information and in accordance with the instructions to Form 10-Q and Rule 10-01 of Regulation S-X. Accordingly, they do not include all of the information and footnotes required by GAAP for complete financial statements. The unaudited interim consolidated financial statements have been prepared on the same basis as the annual financial statements. In the opinion of management, the accompanying unaudited condensed consolidated financial statements reflect all adjustments (consisting only of normal recurring adjustments) considered necessary for a fair presentation. These financial statements should be read in conjunction with the audited financial statements and notes thereto for the preceding fiscal year contained in the Company's Annual Report on Form 10-K filed on February 26, 2016 with the United States Securities and Exchange Commission (SEC).

The results of operations for the three and six months ended June 30, 2016 are not necessarily indicative of the results to be expected for the year ending December 31, 2016. The condensed consolidated balance sheet as of December 31, 2015 has been derived from audited financial statements at that date but does not include all of the information required by GAAP for complete financial statements.

Use of Estimates

The preparation of condensed consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, disclosure of contingent liabilities, and the reported amounts of expenses in the condensed consolidated financial statements and the accompanying notes. Management bases its estimates on historical experience and on various other market-specific and relevant assumptions that management believes to be reasonable under the circumstances. Actual results could differ from those estimates.

Revenue Recognition

The Company recognizes revenue when persuasive evidence of an arrangement exists, delivery has occurred, the price is fixed or determinable, and collectability is reasonably assured. Revenue is recognized once all revenue recognition criteria are met.

During the three months ended June 30, 2016, the Company recognized revenue from sales of rhGUS (UX003) on a "named patient" basis which are allowed in certain European countries prior to the commercial approval of the product in the territory. Due to the Company's limited sales and collection history, to date, revenue has been recognized upon receipt of payment.

Recently Issued Accounting Pronouncements

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)*, which requires an entity that is a lessee to recognize the assets and liabilities arising from leases on the balance sheet. This guidance also requires disclosures about the amount, timing, and uncertainty of cash flows arising from leases. This guidance is effective for annual reporting periods beginning after December 15, 2018, and interim periods within those annual periods, using a modified retrospective approach, and early adoption is permitted. The Company is evaluating the effect that this guidance will have on its Consolidated Financial Statements and related disclosures.

In March 2016, the FASB issued ASU No. 2016-09, *Compensation — Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting*, which simplifies several aspects of the accounting for employee share-based payments, including

income tax consequences, application of award forfeitures to expense, classification on the statement of cash flows, and classification of awards as either equity or liabilities. This guidance is effective for annual reporting periods beginning after December 15, 2016, and interim periods within those annual periods. The Company is evaluating the effect that this guidance will have on its Consolidated Financial Statements and related disclosures.

3. Fair Value Measurements

Financial assets and liabilities are recorded at fair value. The carrying amount of certain financial instruments, including cash and cash equivalents, accounts payable, and accrued liabilities approximate fair value due to their relatively short maturities. Assets and liabilities recorded at fair value on a recurring basis in the condensed consolidated balance sheets are categorized based upon the level of judgment associated with the inputs used to measure their fair values. Fair value is defined as the exchange price that would be received for an asset or the exit price that would be paid to transfer a liability in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. The authoritative guidance on fair value measurements establishes a three-tier fair value hierarchy for disclosure of fair value measurements as follows:

Level 1—Inputs are unadjusted, quoted prices in active markets for identical assets or liabilities at the measurement date;

Level 2—Inputs are observable, unadjusted quoted prices in active markets for similar assets or liabilities, unadjusted quoted prices for identical or similar assets or liabilities in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the related assets or liabilities; and

Level 3—Unobservable inputs that are significant to the measurement of the fair value of the assets or liabilities that are supported by little or no market data.

The following tables set forth the fair value of the Company's financial assets remeasured on a recurring basis based on the three-tier fair value hierarchy (in thousands):

	June 30, 2016			
	Level 1	Level 2	Level 3	Total
Financial Assets:				
Money market funds	$ 19,616	$ —	$ —	$ 19,616
Corporate bonds	—	289,373	—	289,373
Asset-backed securities	—	33,201	—	33,201
U.S. Government Treasury and agency securities	13,994	59,197	—	73,191
Commercial paper	—	11,958	—	11,958
Total financial assets	$ 33,610	$ 393,729	$ —	$ 427,339

	December 31, 2015			
	Level 1	Level 2	Level 3	Total
Financial Assets:				
Money market funds	$ 53,254	$ —	$ —	$ 53,254
Corporate bonds	—	370,445	—	370,445
Asset-backed securities	—	29,302	—	29,302
U.S. Government Treasury and agency securities	—	47,452	—	47,452
Commercial paper	—	13,887	—	13,887
Total financial assets	$ 53,254	$ 461,086	$ —	$ 514,340

4. Balance Sheet Components

Cash Equivalents and Investments

The fair values of cash equivalents, short-term investments, and long-term investments classified as available-for-sale securities, consisted of the following (in thousands):

	June 30, 2016			
		Gross Unrealized		
	Amortized Cost	Gains	Losses	Estimated Fair Value
Money market funds classified as cash equivalents	$ 19,616	$ —	$ —	$ 19,616
Corporate bonds classified as cash equivalents	20,970	—	(2)	20,968
Commercial paper classified as short-term investments	11,958	—	—	11,958
Corporate bonds classified as short-term investments	240,909	103	(43)	240,969
Asset-backed securities classified as short-term investments	33,184	21	(4)	33,201
U.S. Government Treasury and agency securities classified as short-term investments	50,581	25	—	50,606
Corporate bonds classified as long-term investments	27,343	93	—	27,436
U.S. Government Treasury and agency securities classified as long-term investments	22,539	46	—	22,585
Total	$ 427,100	$ 288	$ (49)	$ 427,339

	December 31, 2015			
		Gross Unrealized		
	Amortized Cost	Gains	Losses	Estimated Fair Value
Money market funds classified as cash equivalents	$ 53,254	$ —	$ —	$ 53,254
Corporate bonds classified as cash equivalents	18,403	—	(4)	18,399
Commercial paper classified as short-term investments	13,887	—	—	13,887
Corporate bonds classified as short-term investments	282,386	9	(397)	281,998
Asset-backed securities classified as short-term investments	15,019	—	(27)	14,992
U.S. Government Treasury and agency securities classified as short-term investments	32,628	—	(77)	32,551
Corporate bonds classified as long-term investments	70,309	2	(263)	70,048
Asset-backed securities classified as long-term investments	14,337	—	(27)	14,310
U.S. Government Treasury and agency securities classified as long-term investments	14,985	—	(84)	14,901
Total	$ 515,208	$ 11	$ (879)	$ 514,340

At June 30, 2016, the remaining contractual maturities of available-for-sale securities were less than three years. There have been no significant realized gains or losses on available-for-sale securities for the periods presented.

Accrued Liabilities

Accrued liabilities consist of the following (in thousands):

	June 30, 2016	December 31, 2015
Research and clinical study expenses	$ 11,122	$ 9,764
Payroll and related expenses	8,980	9,423
Other	4,612	5,597
Total accrued liabilities	$ 24,714	$ 24,784

5. License and Research Agreements

Kyowa Hakko Kirin Collaboration and License Agreement

In August 2013, the Company entered into a collaboration and license agreement with Kyowa Hakko Kirin Co., Ltd. (KHK), which was amended in August 2015. Under the terms of this collaboration and license agreement, the Company and KHK will collaborate on the development and commercialization of certain products containing KRN23, an antibody directed towards FGF23, in the field of orphan diseases in the United States and Canada, or the profit share territory, and in the European Union, Switzerland, and Turkey, or the European territory, and the Company will have the right to develop and commercialize such products in the field of orphan diseases in Mexico and Central and South America, or Latin America. In the field of orphan diseases, and except for ongoing studies being conducted by KHK, the Company will be the lead party for development activities in the profit share territory and in the European territory until the applicable transition date; the Company will also be the lead party for core development activities conducted in Japan and Korea, provided that the core development plan related to Japan and Korea shall be limited to clinical trials mutually agreed to by the Company and KHK. The Company will share the costs for development activities in the profit share territory and the European territory conducted pursuant to the development plan before the applicable transition date equally with KHK, and KHK shall be responsible for 100% of the costs for development activities in Japan and Korea. On the applicable transition date in the profit share territory and the European territory, KHK will become the lead party and be responsible for the costs of the development activities. However, the Company will continue to share the costs of the studies commenced prior to the applicable transition date equally with KHK. The Company has the primary responsibility for conducting certain research and development services. The Company is obligated to provide assistance in accordance with the agreed upon development plan as well as participate on various committees. If KRN23 is approved, the Company and KHK will share commercial responsibilities and profits in the profit share territory until the applicable transition date, KHK will commercialize KRN23 in the European territory, and the Company will develop and commercialize KRN23 in Latin America. KHK will manufacture and supply KRN23 for clinical use globally and will manufacture and supply KRN23 for commercial use in the profit share territory and Latin America.

The Company is accounting for the agreement as a collaboration arrangement as defined in ASC 808, *Collaborative Agreements*. The Company's expenses were reduced by $6.1 million and $2.1 million for the three months ended June 30, 2016 and 2015, and $11.0 million and $3.6 million for the six months ended June 30, 2016 and 2015, respectively, for its share of the costs as research and development. As of June 30, 2016 and December 31, 2015, the Company had receivables in the amount of $6.1 million and $3.8 million, respectively, for this collaboration arrangement.

6. Stock-Based Awards

2014 Incentive Plan

In 2014, the Company adopted the 2014 Incentive Plan (the 2014 Plan), which became effective upon the closing of the Company's IPO in February 2014. The 2014 Plan provides for automatic annual increases in shares available for grant, beginning on January 1, 2015 through January 1, 2024. As of June 30, 2016, there were 1,053,702 shares reserved under the 2014 Plan for the future issuance of equity awards. The Company also had 1,380,922 shares reserved for the 2014 Employee Stock Purchase Plan, for which no shares had been issued.

Stock-Based Compensation Expense

The table below sets forth the functional classification of stock-based compensation expense, net of estimated forfeitures, for the periods presented (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2016	2015	2016	2015
Research and development	$ 6,495	$ 3,132	$ 13,070	$ 4,973
General and administrative	4,365	1,959	8,007	2,526
Total stock-based compensation	$ 10,860	$ 5,091	$ 21,077	$ 7,499

7. Net Loss Per Share

Basic net loss per share has been computed by dividing the net loss by the weighted-average number of shares of common stock outstanding during the period. Diluted net loss per share is calculated by dividing net loss by the weighted-average number of shares of common stock and potential dilutive securities outstanding during the period.

The following weighted-average outstanding common stock equivalents were excluded from the computation of diluted net loss per share for the periods presented because including them would have been antidilutive:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2016	2015	2016	2015
Stock options to purchase common stock	4,150,911	2,974,250	3,989,477	2,836,548
Unvested restricted stock units	338,964	93,013	275,112	63,434
Common stock warrants	149,700	159,296	149,700	241,824
	4,639,575	3,226,559	4,414,289	3,141,806

8. Subsequent Events

Takeda License and Collaboration and Purchase Agreements

On June 6, 2016, the Company executed a license and collaboration agreement with Takeda Pharmaceutical Company Limited (“Takeda”) that became effective on July 21, 2016 upon expiration of a required Hart-Scott-Rodino Antitrust Act filing review period. Pursuant to the agreement, the Company obtained an exclusive license for a pre-clinical compound from Takeda in a pre-determined field of use, as well as an option to license additional Takeda product candidates. The Company and Takeda established a five-year research collaboration whereby the Company is responsible for substantially all development pursuant to an agreed research plan, and the Company will bear the cost of development activities (except certain validation development activities relating to candidate products, for which Takeda will bear all costs) for option product candidates that the Company elects as part of the collaboration. The Company also granted Takeda an exclusive option for Asian rights to any licensed products resulting from the collaboration as well as an option to exclusively license one of the Company’s products for development and commercialization in Japan. If Takeda exercises any of its option rights to license a compound pursuant to the agreement, the parties will enter into a separate royalty-bearing license on customary terms to be negotiated.

For the initial licensed product from Takeda, the agreement provides for royalties payable to Takeda in the high-single digits to low-teens on tiered net sales levels of products during the royalty term. The Company may be required to make future milestone payments to Takeda of up to $7.5 million for development milestones, $75.0 million for regulatory milestones and $150.0 million for commercial milestones.

In connection with the license and collaboration agreement, the Company and Takeda also entered into a common stock purchase agreement whereby Takeda purchased in July 2016, 374,590 shares of the Company’s common stock for total consideration of $40.0 million for an effective per-share price of $106.78. Beginning 3 months after the effective date of the collaboration, the Company has the option, exercisable in its sole discretion, to require Takeda to purchase an additional $25.0 million in shares of common stock at the then-current 30-day volume weighted average price (the “VWAP”), with such right expiring on the first anniversary of the effective date of the collaboration. Contingent upon meeting certain milestones as noted in the collaboration agreement, the Company has a second option, exercisable in its sole discretion, to require Takeda to purchase an additional $10.0 million in shares of common stock at the then-current 30-day VWAP. Pursuant to the terms of the common stock purchase agreement, Takeda is subject to a 180-day lock-up provision related to the initial shares, is subject to a five-year standstill (subject to customary exceptions or release) and has registration rights for the shares.

Underwritten Future Public Offering

On July 1, 2016, we entered into an At-The-Market, or ATM, sales agreement, with Cowen and Company, LLC (Cowen), under which we may offer and sell our common stock having aggregate proceeds of up to $150.0 million from time to time through Cowen as our sales agent.

We will pay Cowen a commission, or allow a discount, for its services in acting as agent and/or principal in the sale of common stock, of up to 3.0% of the gross sales price per share of all shares sold through it as agent under the sales agreement.

Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with the accompanying unaudited consolidated financial statements and related notes in Item 1 and with the audited consolidated financial statements and the related notes included in our Annual Report on Form 10-K for the year ended December 31, 2015.

Overview

We are a clinical-stage biopharmaceutical company focused on the identification, acquisition, development, and commercialization of novel products for the treatment of serious rare and ultra-rare diseases, with a focus on serious, debilitating genetic diseases. We target diseases for which the unmet medical need is high, the biology for treatment is clear, and for which there are no currently approved therapies. Since our inception in 2010, we have in-licensed potential treatments for multiple rare genetic disorders. Our strategy, which is predicated upon time- and cost-efficient drug development, allows us to pursue multiple programs in parallel with the goal of delivering safe and effective therapies to patients with the utmost urgency.

Our current clinical-stage pipeline consists of two product categories: biologics (including a monoclonal antibody and an enzyme replacement therapy); and small-molecule substrate replacement therapies. Enzymes are proteins that the body uses to process materials needed for normal cellular function, and substrates are the materials upon which enzymes act. When enzymes or substrates are missing, the body is unable to perform its normal cellular functions, often leading to significant clinical disease. Several of our therapies are intended to replace deficient enzymes or substrates.

Our biologics pipeline includes the following product candidates in clinical development for the treatment of three diseases:

- KRN23, or UX023, is an antibody targeting fibroblast growth factor 23, or FGF23, in development for the treatment of X-linked hypophosphatemia, or XLH, a rare genetic disease that impairs bone growth. We are developing KRN23 pursuant to our collaboration with Kyowa Hakko Kirin Co., Ltd., or KHK. KHK has completed one Phase 1 study, one Phase 1/2 study, and one longer-term Phase 1/2 study of KRN23 in adults with XLH. We initiated a Phase 2 pediatric study in July 2014 and completed enrollment in a 134-patient Phase 3 adult study in July 2016.
- KRN23 is also being developed for the treatment of tumor-induced osteomalacia, or TIO. TIO results from typically benign tumors that produce excess levels of FGF23, which can lead to severe hypophosphatemia, osteomalacia, fractures, fatigue, bone and muscle pain, and muscle weakness. We initiated a Phase 2 study of KRN23 in adult inoperable TIO patients in March 2015.
- Recombinant human beta-glucuronidase, or rhGUS or UX003, is an enzyme replacement therapy we are developing for the treatment of mucopolysaccharidosis 7, or MPS 7, a rare lysosomal storage disease that often leads to multi-organ dysfunction, pervasive skeletal disease, and death. In July 2016, we announced that the study met its primary endpoint of reduction in urinary GAG excretion and provides evidence of clinical improvement.

Our substrate replacement therapy pipeline includes the following product candidates in clinical development for the treatment of three diseases:

- UX007 is a synthetic triglyceride with a specifically designed chemical composition being studied in an open-label Phase 2 study for the treatment of long-chain fatty acid oxidation disorders, or LC-FAOD, from which interim results were recently reported. LC-FAOD is a set of rare metabolic diseases that prevents the conversion of fat into energy and can cause low blood sugar, muscle rupture, and heart and liver disease. The Company is planning for a Phase 3 study that it expects to initiate in 2017 after discussions with regulatory authorities.
- UX007 is also in a Phase 2 study for the treatment of glucose transporter type-1 deficiency syndrome, or Glut1 DS, a rare metabolic disease of brain energy deficiency that is characterized by seizures, developmental delay, and movement disorder. The Phase 2 study in Glut1 DS patients with seizures continues to enroll patients. A Phase 3 study in the movement disorder phenotype of Glut1 DS is expected to begin in the second half of 2016.
- Aceneuramic acid extended-release, or Ace-ER or UX001, is an extended-release form of aceneuramic acid in a Phase 2 extension study for the treatment of GNE myopathy, a neuromuscular disorder that causes muscle weakness and wasting. We filed a Marketing Authorization Application, or MAA, seeking conditional approval from the European Medicines Agency, or EMA, for the use of Ace-ER in the treatment of GNE myopathy with this Phase 2 data. The Committee for Orphan Medicinal Products for Human Use (CHMP) opinion on the conditional marketing authorization application is expected in the second half of 2016, and a decision from the European Commission is expected in the first half of 2017. We also completed enrollment in a Phase 3 study in July 2016.

Clinical Product Candidates

The following table summarizes our current clinical-stage product candidate pipeline:

KRN23 (UX023) for the treatment of XLH

KRN23 is a fully human monoclonal antibody administered via subcutaneous injection that is designed to bind and reduce the biological activity of FGF23 to increase abnormally low phosphate levels in patients with XLH. Patients with XLH have low serum phosphate levels due to excessive phosphate loss into the urine, which is directly caused by the effect on kidney function of excess FGF23 production in bone cells. Low phosphate levels lead to poor bone mineralization and a variety of clinical manifestations, including rickets, leading to bowing and other skeletal deformities, short stature, bone pain and fractures, and muscle weakness. There is no approved drug therapy or treatment for the underlying cause of XLH. Most patients are managed using frequently dosed oral phosphate replacement and vitamin D therapy, which can lead to significant side effects. Oral phosphate/vitamin D replacement therapy requires extremely close monitoring due to the potential for excessive phosphate levels and secondary increases in calcium, which can result in severe damage to the kidneys from excess calcium phosphate deposits and other complications. Additionally, some patients are unable to tolerate the regimen due to the chalky stool that results from taking large amounts of oral phosphate or the high frequency of dosing required. The U.S. Food and Drug Administration (FDA) has granted Fast Track Designation to the KRN23 program for the treatment of XLH, and Breakthrough Therapy Designation for pediatric patients one year of age or older.

In August 2013, we entered into a collaboration agreement with KHK, as amended in August 2015, to jointly develop and commercialize KRN23. KHK has conducted one Phase 1 study, one Phase 1/2 study, and one longer-term Phase 1/2 study of KRN23 in adults with XLH. Results from a four-month Phase 1/2 study in 28 adult XLH patients and a subsequent twelve-month Phase 1/2 study of KRN23 in 22 patients were presented at the 2014 ICE/ENDO joint meeting of The Endocrine Society and the International Congress on Endocrinology in June 2014 and the American Society for Bone and Mineral Research (ASBMR) Annual Meeting in September 2014, respectively.

In July 2014, we announced the first patient screened and enrolled in the Phase 2 pediatric study of KRN23 in patients ages 5 to 12 years with XLH. The study consists of a 16-week individual dose-titration period followed by a 48-week treatment period, for a total of 64 weeks. Patients were divided into three cohorts of escalating starting dose levels of KRN23 with either monthly or biweekly dosing regimens. At the end of the 16-week dose-titration period, patients were allowed to continue to receive dose increases in order to reach the individually optimized dose of KRN23 on a monthly or biweekly basis for the 48-week treatment period. In late 2014, we completed enrollment of 36 patients. Based on positive 16-week data, we decided to enroll an additional 16 patient cohort with patients who had more severe disease at baseline (based on their Thacher Rickets Severity Scoring System (RSS) knee score >1.5). Patients for the Phase 2 study were enrolled at nine global centers of excellence in XLH. The primary objectives of the study are to identify a dose and dosing regimen and to establish the safety profile of treatment with KRN23 in pediatric XLH patients. We are also assessing preliminary clinical effects of KRN23 treatment on bone health and deformity as measured by radiographic assessments, growth, muscle strength, and motor function, as well as markers of bone health and patient-reported outcomes of pain, disability, and quality of life.

In December 2015, we released interim data through 40 weeks from the first 36 patients in this study. Thirty five of 36 patients had previously been on standard of care (oral phosphate/vitamin D therapy) for an average of 6.6 years (range: 0 - 11.7 years). Patient demographics were well balanced between the biweekly (n=18) and monthly (n=18) dose groups. Rickets were evaluated via two scoring systems – the RSS and the Radiographic Global Impression of Change (RGI-C). A subset of patients (n=18; 9 dosed biweekly and 9 dosed monthly) were pre-specified as having high rickets severity (greater bone disease) if their baseline total RSS scores were $\geq$ 1.5. For the responder analysis using total RSS, responders were pre-defined as those patients who had baseline total RSS scores > 1.0 and had 1.0 or more reduction at Week 40 which is considered a significant improvement.

Overall, in all patients (n=36), the mean total RSS score decreased from 1.43 at baseline to 1.00 at 40 weeks (-0.43; 30% reduction; p=0.0076), and 61% of the patients (14/23) were responders. In all the high severity patients (n=18), the mean total rickets score decreased from 2.31 at baseline to 1.22 at 40 weeks (-1.08; 47% reduction; p<0.0001), and 72% of these patients were responders (13/18). In patients who were dosed bi-weekly (n=18), the mean total RSS score decreased from 1.53 at baseline to 0.86 at 40 weeks (-0.67 points; 44% reduction; p=0.0126), and 75% of the patients (9/12) were responders. In the high severity patients who were dosed bi-weekly (n=9), the mean total rickets score decreased from 2.44 at baseline to 1.00 at 40 weeks (-1.44 points; 59% reduction; p<0.0001), and 89% of these patients were responders (8/9). In patients who were dosed monthly (n=18), the mean total rickets score decreased from 1.33 at baseline to 1.14 at 40 weeks (-0.19 points; 14% reduction), and 46% of the patients (5/11) were responders. In the high severity patients who were dosed monthly (n=9), the mean total RSS score decreased from 2.17 at baseline to 1.44 at 40 weeks (-0.72; 33% reduction) and 56% of these patients (5/9) were responders.

Overall, all patients (n=36) experienced a mean improvement in RGI-C score of +1.38 (p<0.0001) and those patients who were severe (n=18) experienced a mean improvement of +1.85 (p<0.0001) at 40 weeks. Within the high severity subset, 67% (12/18) experienced substantial healing (score >2). Patients who were dosed bi-weekly (n=18) experienced a mean improvement in RGI-C score of +1.56 (p<0.0001). Those patients with high severity rickets (n=9) experienced a mean improvement of +2.00 (p<0.0001) at 40 weeks (substantial healing) and 89% (8/9) experienced substantial healing (score >2). Patients who were dosed monthly (n=18) experienced a mean improvement in RGI-C score of +1.20. The patients with high severity rickets (n=9) experienced a mean improvement of +1.70 at 40 weeks and 44% (4/9) experienced substantial healing (score >2).

Patients with walking impairment at baseline (defined by < 80% predicted normal walk distance in the six minute walk test, or 6MWT; n=14) achieved a mean increase of 80 meters (an approximate 20% increase from baseline) in the 6MWT at week 40. Both high and low rickets-severity patients with walking impairments at baseline experienced a mean improvement in meters walked at week 40. Functional disability scores were measured with the Pediatric Orthopedic Society North America/Pediatric Outcome Data Collection Instrument (POSNA/PODCI). When evaluating the global score across all five domains in those patients with substantial impairment at baseline (n=15) or with severe rickets at baseline (n=18), a substantial mean improvement was observed of about one standard deviation or greater in both dose groups. The Pain/Comfort and Sports/Physical Functioning domains were the most affected at baseline and also substantially improved in these severely affected subjects treated in both dose groups.

The most common treatment-related adverse event reported by preferred term was injection site reaction in 39% of patients. All of these reactions were considered mild. All other treatment-related adverse events were considered mild. There was one serious adverse event considered possibly treatment-related. This was a patient with fever and muscle pain who improved without complication and is still in the trial. There have been no deaths or discontinuations from the study for any reason. No clinically meaningful changes were observed in mean serum calcium, urinary calcium and in serum intact parathyroid hormone. None of the patients had serum phosphorus levels above the upper limit of normal at any time point. No clinically significant changes were observed in renal ultrasounds pre- and post-treatment. All patients demonstrated increases in serum phosphorus that were consistent with what had been observed previously reaching the low normal or just below normal range. Across both dose groups there were mean increases in both the renal phosphate reabsorption (TmP/GFR) and in serum 1,25 dihydroxy vitamin D levels through 40 weeks of treatment.

Additional data from the pediatric Phase 2 study are expected in the second half of 2016. We expect to have 40-week data from all 52 patients, including rickets scores (RSS and RGI-C), and 64-week data from 36 patients, including height-growth velocity. We and our partner, KHK, plan to file an application near the end of 2016 seeking conditional marketing authorization in the EU based on these data. In addition, we plan to proceed with a pediatric Phase 3 study in mid-2016. The study will utilize RGI-C as the primary endpoint and will include a reference arm of oral phosphare and vitamin D.

We are also continuing to develop KRN23 in adults with XLH. We have initiated a long-term, open-label Phase 2b extension study of KRN23 in adult XLH patients who had previously participated in the studies conducted by KHK. In July 2016, we completed enrollment of 134 patients in a Phase 3 study of KRN23 for the treatment of adults with XLH. The Phase 3 study is an international, randomized, double-blind, placebo-controlled clinical study assessing the efficacy and safety of monthly KRN23 in adult XLH patients. The primary endpoint of the study is serum phosphorus levels through 24 weeks, and the key secondary endpoint is the Brief Pain Inventory Question 3 (pain at its worst in the last 24 hours) at Week 24. Other secondary endpoints include patient reported outcomes assessing skeletal pain, stiffness, fatigue, motor function, and quality of life in these patients. A 48-week open-label bone quality study in approximately 14 adult XLH patients evaluating the potential impact of KRN23 on the underlying osteomalacia via bone biopsy is currently enrolling patients.

KRN23 (UX023) for the treatment of TIO

We are also developing KRN23 for the treatment of TIO. TIO results from typically benign tumors that produce excess levels of FGF23, which can lead to severe hypophosphatemia, osteomalacia, bone fractures, fatigue, bone and muscle pain, and muscle weakness. There are cases in which resection of the tumor is not feasible or recurrence of the tumor occurs after resection. In patients for whom the tumor is inoperable, the current standard of care consists of oral phosphate and/or vitamin D replacement. The efficacy of this treatment is often limited, as it does not treat the underlying disease and its benefits must be balanced with monitoring for potential risks such as nephrocalcinosis, hypercalciuria, and hyperparathyroidism. We are enrolling patients in an open-label, proof of concept Phase 2 clinical study.

This Phase 2 study evaluates safety and efficacy in approximately 15 adult inoperable patients. The primary objectives of the study are to establish the dose and assess the safety profile of treatment with KRN23 in adults with TIO. Patients receive subcutaneous injections of KRN23 once every four weeks for 48 weeks. All patients begin treatment with KRN23 at a starting dose of 0.3 mg/kg. Doses are then titrated in an effort to achieve a target fasting serum phosphorus range of 2.5 to 4.0 mg/dL. After completing the initial 48-week treatment period of the study, patients may continue into a planned treatment extension period in which they would receive KRN23 treatment for up to an additional 96 weeks. The co-primary endpoints include: the proportion of patients achieving mean peak serum phosphorus levels above the lower limit of normal (LLN; 2.5 mg/dL), as averaged between baseline and week 24; and the percent change from baseline in excess osteoid after 48 weeks of treatment. Preliminary clinical effects of KRN23 treatment are evaluated by radiographic assessments, muscle strength, walking ability, and patient-reported measures of pain, disability, and quality of life. Markers of bone health and changes in serum phosphorus and other biochemical measures are also followed.

In April 2016 we released interim data from the first eight patients in this study. Before KRN23 treatment and after washout with any oral phosphate treatment, the mean serum phosphorus level was 1.7 mg/dL, below the lower limit of normal of 2.5 mg/dL. After KRN23 treatment began, six of the eight patients achieved normalization of their serum phosphorus levels. The dose continues to be titrated up in one of the two patients whose serum phosphorus levels increased but had not yet entered the normal range. Renal phosphate reabsorption (TmP/GFR) and serum 1,25 dihydroxy vitamin D levels also increased in seven of the eight patients. One of these patients did not demonstrate an improvement in these markers. Overall, the improvement in serum phosphorus and other bone mineral metabolism measures observed in this study to date is generally consistent with what has been observed in studies of KRN23 in pediatric and adult patients with XLH. Of the eight patients enrolled, the two patients who completed 24 weeks of treatment showed an improvement in bone mineral density, and one of these two patients showed early evidence of fracture resolution, determined via bone scan.

There have been no serious adverse events. Treatment-emergent adverse events were observed in seven patients. Treatment-emergent adverse events occurring in two or more patients were primarily musculoskeletal disorders including pain in extremity, arthralgia, and musculoskeletal pain consistent with the symptoms typically seen in patients with TIO and epidermal nevus syndrome (ENS). Two of the eight patients had treatment-related adverse events that were possibly/probably related, including Vitamin D deficiency and rash, both of which were mild in grade. No injection site reactions were observed. Two subjects reported symptoms suggestive of worsening pre-existing restless leg syndrome.

No clinically meaningful changes were observed in mean serum calcium, urinary calcium and in serum intact parathyroid hormone. One patient had serum phosphorus levels above the upper limit of normal at three weeks of treatment that returned to the normal range by week four after dose reduction, and has remained in the normal range. Additional bone data is expected in the second half of 2016.

rhGUS (UX003) for the treatment of MPS 7

rhGUS is an intravenous, or IV, enzyme replacement therapy for the treatment of MPS 7, also known as Sly Syndrome. Patients with MPS 7 suffer from severe cellular and organ dysfunction that typically leads to death in the teens or early adulthood. MPS 7 is caused by a deficiency of the lysosomal enzyme beta-glucuronidase, which is required for the breakdown of certain complex carbohydrates known as glycosaminoglycans, or GAGs. The inability to properly break down GAGs leads to their accumulation in many tissues, resulting in a serious multi-system disease. Patients with MPS 7 may have abnormal coarsened facial features, enlargement of the liver and spleen, airway obstruction, lung disease, cardiovascular complications, joint stiffness, short stature, and a skeletal disease known as dysostosis multiplex. In addition, many patients experience progressive lung problems as a result of airway obstruction and mucous production, often leading to sleep apnea and pulmonary insufficiency, and eventually requiring tracheostomy. There are currently no approved drug therapies for MPS 7.

We licensed exclusive worldwide rights to rhGUS-related know-how and cell lines from Saint Louis University in November 2010. We have conducted preclinical studies to support the chronic IV administration of rhGUS. Administration of rhGUS resulted in substantial distribution of enzyme, as well as reduction in tissue pathology in a wide variety of tissues, including the liver, spleen, lung, heart, kidney, muscle, bone, and brain. No adverse toxicology related to rhGUS was noted in these studies.

In December 2013, we initiated an open-label, Phase 1/2 study in the United Kingdom to evaluate the safety, tolerability, efficacy, and dose of IV administration of rhGUS every other week in three patients with MPS 7. Results from the 12-week analysis evaluating 2 mg/kg of rhGUS every other week were presented in September 2014 at the Society for the Study of Inborn Errors of Metabolism, or SSIEM, Annual Symposium and showed a decline in urinary glycosaminoglycans, or GAG excretion of approximately 40-50% from baseline. After the initial 12 weeks, the study entered a dose-exploration phase in which patients were treated with a lower and then higher dose of rhGUS. The 36-week results, which were presented in February 2015 at the Annual WORLD Symposium, showed a greater change in urinary GAG excretion at the higher 4 mg/kg dose of rhGUS, with a mean urinary GAG reduction of approximately 60%.

Sustained decreases in liver size were observed in the two patients who had enlarged livers at baseline, and an improvement in pulmonary function was observed in the one patient who was able to perform the evaluations. Improvements were also observed in the MPS Health Assessment Questionnaire measure of functional capabilities and in the Physician Global Impression of Change scale of overall health status in this open-label study.

No serious adverse events or infusion-associated reactions were observed in the study. The most common adverse events were consistent with the symptoms of MPS 7 or related to intravenous administration of the investigational therapy, including respiratory disorders, infections, and arthralgia.

We initiated a Phase 3 global, randomized, placebo-controlled, blind-start clinical study in December 2014. The Phase 3 study was designed to assess the efficacy and safety of rhGUS in 12 patients between five and 35 years of age. Patients were randomized to one of four groups. One cohort began rhGUS therapy immediately, while the other three started on placebo and crossed over to rhGUS at different predefined time points in a blinded manner. This study design generated treatment data from all 12 patients. Based on data from the Phase 1/2 study, patients were dosed with 4 mg/kg of rhGUS every other week for up to a total of 48 weeks, and all groups received a minimum of 24 weeks of treatment with rhGUS.

The primary objective of the study is to determine the efficacy of rhGUS as determined by the percent reduction in urinary GAG excretion after 24 weeks of treatment. The Phase 3 study is also evaluating as secondary endpoints the safety and tolerability of rhGUS, pulmonary function, walking, stair climb, shoulder flexion, fine and gross motor function, hepatosplenomegaly, cardiac size and function, visual acuity, patient and caregiver assessment of most significant clinical problems, global impressions of change, a multi-domain responder index, and other endpoints.

In July 2016, we announced that the study met its primary endpoint of reducing urinary GAG (dermatan sulfate) excretion after 24 weeks of treatment, demonstrating a reduction from baseline of 64.8 percent ($p<0.0001$). The Multi-domain Responder Index (MDRI) score at 24 weeks of treatment, a secondary endpoint, demonstrated an overall mean improvement (±SD) of +0.5 domains (±0.80) ($p=0.0527$). Six of the 12 patients had an improvement in their MDRI score of +1 or more. Five patients demonstrated no worsening of this progressive disease, or an MDRI score of 0. One patient had an MDRI score of -1. The MDRI is a summation of scores from each of the following domains: the six-minute walk test (6MWT), forced vital capacity (FVC), shoulder flexion, visual acuity, and the Bruininks-Oseretsky Test of Motor Proficiency (BOT-2) fine motor and gross motor function. For the 6MWT, the improvement (±SE) was 20.8 (±16.75) meters at 24 weeks of treatment based on the estimates from 9 patients who had any change from baseline data. Three of these patients demonstrated an improvement of a magnitude equal or greater than the minimally important difference (MID) with increases of 65 meters, 80 meters and 83 meters at 24 weeks compared to baseline. For the fatigue scores, four patients improved at or above the MID level after 24 weeks of treatment and nine of 12 showed improvement at some point during the study. All patients experienced treatment emergent adverse events, which were generally mild to moderate in severity. Six of the eight patients with infusion associated reactions (IARs) on rhGUS treatment had events involving the IV catheter. There were two patients that each had a single hypersensitivity-type IAR, including one Grade 3 treatment-related anaphylactoid serious adverse event (SAE) that resulted from an infusion rate error. The second patient had mild fever and diaphoresis that resolved without treatment. No patients demonstrated recurring hypersensitivity reactions to infusions. There was a second SAE that was a Grade 2 unrelated event from an accidental injury. There were no deaths and no treatment discontinuations or missed infusions due to AEs. Seven of the 12 patients developed anti-rhGUS antibodies, which were not associated with immune-mediated AEs.

Based on the data from the Phase 3 study, we plan to meet with the FDA and EMA this year to discuss our plans to submit regulatory filings in the first half of 2017.We previously obtained feedback from the FDA and the EMA regarding the design of the Phase 3 study. The FDA stated that their evaluation of the pivotal Phase 3 study will be based on the totality of the data on a patient-by-patient basis and advised against the declaration of a primary endpoint. The EMA has agreed that approval under exceptional circumstances could be possible based upon a single positive placebo-controlled pivotal study in approximately 12 patients using urinary GAG levels as a surrogate primary endpoint, provided the data was strongly supportive of a favorable benefit/risk ratio. The EMA requested that some evidence or trend in improvement in clinical endpoints be observed to support the primary endpoint, but recognized that a statistically significant result on clinical endpoints was unlikely given the small number of patients expected to be enrolled in the study.

In August 2015 we initiated a study of rhGUS in MPS 7 patients under the age of five years, including potentially younger infants born with hydrops fetalis. These hydropic infants can die within a few months to one year of birth, but enzyme replacement therapy might be able to reduce GAG storage and improve health in these patients. The Phase 2 open-label study will assess the safety, tolerability, and efficacy of rhGUS in up to seven pediatric patients under five years old.

We are also supplying rhGUS to investigators who are treating patients under emergency investigational new drug, or eIND, applications and other expanded access programs. Results following 24 weeks of treatment of the first eIND patient were announced in September 2014 and published in Molecular Genetics and Metabolism in February 2015.

UX007 for the treatment of LC-FAOD

We are developing UX007 for oral administration intended as a substrate replacement therapy for patients with LC-FAOD. UX007 is a purified, pharmaceutical-grade form of triheptanoin, a specially designed synthetic triglyceride compound, created via a multi-step chemical process. UX007 is a medium odd-chain triglyceride of seven-carbon fatty acids designed to provide substrate replacement for fatty acid metabolism and restore production of energy. Patients with LC-FAOD have a deficiency that impairs the ability to produce energy from fat, which can lead to depletion of glucose in the body, and severe liver, muscle, and heart disease, as well as death. There are currently no approved drugs or treatments specifically for LC-FAOD. The current standard of care for LC-FAOD includes diligent prevention of fasting combined with the use of low-fat/high-carbohydrate diets, carnitine supplementation in some cases, and medium even-chain triglyceride oil supplementation. Despite treatment with the current standard of care, many patients continue to suffer significant morbidity and mortality.

We licensed certain intellectual property rights for triheptanoin from Baylor Research Institute in August 2012. Triheptanoin has been studied clinically for over a decade in more than a hundred human subjects affected by a variety of diseases. Multiple investigator-sponsored open-label studies suggest clinical improvements with triheptanoin treatment, even for patients who were on standard of care. We presented data at the International Conference of Inborn Errors of Metabolism, or ICIEM, in August 2013 from a retrospective medical record review study assessing the clinical outcome of triheptanoin treatment on LC-FAOD subjects who had been participating in a compassionate use program at the University of Pittsburgh Medical Center. The data showed that treatment with triheptanoin appeared to reduce the frequency and severity of hospitalizations previously experienced by these patients for disease-related causes, including muscle rupture, hypoglycemia, and cardiomyopathy. A reduction in mean total hospital days per year from 17.55 to 5.40 (69%; $p = 0.0242$) was observed after transitioning from standard of care to triheptanoin therapy. These results are clinically important but are derived from a retrospective medical review, and not from a prospective randomized controlled study.

In September 2015, case reports from five infants with moderate or severe cardiomyopathy due to LC-FAOD were presented at the SSIEM Annual Symposium. While on the standard of care medium-chain triglyceride, or MCT, oil, the patients were hospitalized with heart failure that required cardiac support and, in some cases, resuscitation. The patients discontinued MCT oil and then began to receive triheptanoin on an expanded access basis. In patients with known ejection fraction, or EF, values before and after treatment (n=4) the mean EF prior to treatment with triheptanoin was 32% (range: 21% to 44%) and after treatment at last assessment was 66% (range: 55% to 71%). The most common adverse events were gastrointestinal distress, including loose stools. One patient discontinued treatment after approximately 14 weeks due to gastrointestinal symptoms. No other significant tolerance issues or treatment-related adverse events were reported. Four of the patients continue to receive triheptanoin. These data are from an expanded access program and are based on open-label uncontrolled treatment, which limits definitive conclusions about efficacy and safety.

In October 2015, we reported interim data on the acute effects of UX007 that was being evaluated in a Phase 2 study in LC-FAOD patients. The study was single-arm open-label and evaluated 29 pediatric and adult patients across three main symptom groups (musculoskeletal, liver/hypoglycemia, and cardiac). Patients needed to have moderate to severe FAOD with significant disease in at least one of these domains or a frequent medical events history in order to enroll. The study began with a four-week run-in period to assess baseline data while on the standard of care therapy including MCT oil, if applicable. Patients on MCT oil then discontinued it and UX007 was titrated to a target dose of 25-35% of total daily caloric intake. Patients were followed to evaluate the effects of UX007 treatment over 24 weeks on several endpoints, including cycle ergometry performance, 12-minute walk test, liver disease/hypoglycemia, cardiac disease, and quality of life. The 24-week analysis mainly evaluated the acute effects of UX007 on the musculoskeletal aspects of the disease. Patients who opted to continue will be treated for a total of 78 weeks, and rates of major medical events, such as rhabdomyolysis, hypoglycemia and cardiac events, will be monitored and compared to rates for the two years prior to treatment with UX007. The study planned to evaluate the safety and tolerability of UX007 and to determine both the appropriate patient population as well as endpoints for evaluation in a Phase 3 study. The majority of patients enrolled presented with musculoskeletal disease compared to a limited number who presented with liver and cardiac symptoms. Patients spanned a wide age

range from ten months to 58 years old. Prior to initiating treatment with UX007, 27 of the 29 patients were on the standard of care MCT oil therapy. Following discontinuation of MCT oil therapy, the average dose of UX007 through 24 weeks was 30% of total daily caloric intake.

Improvements were observed in both measures of exercise tolerance (cycle ergometry and 12 minute walk test) in musculoskeletal patients who performed the tests. The three areas of evaluation with cycle ergometry included workload (measured in watts produced at a fixed heart rate), respiratory exchange ratio, or RER, a measure of energy supply, and duration of cycling. Patients showed improvements in both workload and duration and no change in RER. At week 24, seven patients (who qualified by age and performed the test at baseline) produced a mean 60% increase in watts over baseline representing a mean increase of +446.8 watts (median: +127.5; min, max: -388, +2438). The mean duration was increased in 3 patients who did not complete all 40 minutes at baseline. Eight qualified patients demonstrated a mean 28% increase of +188 meters (median: 93.5; min, max: -80, +880) at week 18 in the 12-minute walk test. These patients also experienced an improvement in the mean energy expenditure index (a ratio of heart rate per meter walked). The data on the 12 minute walk test and cycle ergometry together support an improvement in muscle function and exercise efficiency in a small number of patients that would need to be confirmed in larger controlled studies. Patients with liver/hypoglycemia and cardiac disease were limited, 3 and 2 respectively, but they qualified for entry due to frequent history of events and will contribute to the event rate measurement over 78 weeks.

Overall, major medical events appeared to decrease in the 25 patients who completed the 24 weeks of treatment when compared to the reported event rate in these patients approximately 18 months prior to treatment with UX007. These data are preliminary and require significantly more time for proper evaluation at the 78 week time-point. The major medical event rate aggregates events related to hypoglycemia, rhabdomyolysis, and cardiomyopathy.

Improvements in patient-reported quality of life scores (SF-12) were observed in adult patients, but no difference was seen in parent-reported scores (SF-10) for pediatric patients. The Peabody Developmental Motor Score (PDMS-2) and the Pediatric Disability Inventory (PEDI-CAT), also showed no impairment in the overall patient population at baseline and no change after 24 weeks.

Four of the 29 enrolled patients discontinued prior to 24 weeks. One patient discontinued due to diarrhea in week 1, which resolved within a few days of discontinuation, and three patients withdrew consent (weeks 1, 8, 8) for reasons not attributed to treatment with UX007. All other patients opted to continue treatment in the extension phase of the study. There have been no deaths. One serious related adverse event of moderate gastroenteritis with vomiting was considered treatment-related. A viral infection was suspected, but the investigator could not rule out cause by UX007 given the proximity to dosing. That patient continues to be treated in the study and maintained dosing throughout the event, which has now resolved. Overall, 18 patients (62%) had treatment-related adverse events, most of which were mild-to-moderate in nature. The most common treatment-related adverse events were diarrhea, abdominal/gastrointestinal pain, and vomiting. Some gastrointestinal events were managed by adjusting dosing or dosing with food. The most common adverse events, including those not deemed treatment-related, were viral infections, gastrointestinal disorders, rhabdomyolysis, fever, and headache.

78-week data, including a comparison of major medical event rates approximately 18 months before and after UX007 treatment, as well as long-term safety and exercise tolerance data, are expected in the second half of 2016. We are planning to initiate a Phase 3 study in LC-FAOD patients in 2017 based on the interim Phase 2 data. The Phase 3 trial design and endpoints continue to be optimized prior to discussion with regulators. Further details are expected to be provided after discussions with regulatory authorities.

UX007 for the treatment of Glut1 DS

We are also developing UX007 for patients with Glut1 DS. Glut1 DS is caused by a mutation affecting the gene that codes for Glut1, which is a protein that transports glucose from the blood into the brain. Because glucose is the primary source of energy for the brain, Glut1 DS results in a chronic state of brain energy deficiency and is characterized by seizures, developmental delay, and movement disorder. There are currently no approved drugs specific to Glut1 DS. The current standard of care for Glut1 DS is the ketogenic diet, an extreme high-fat (70-80% of daily calories as fat)/low-carbohydrate diet, which generates ketone bodies as an alternative energy source to glucose, and one or more antiepileptic drugs. The ketogenic diet can be effective in reducing seizures but compliance can be difficult, and the effectiveness of the diet in the treatment of developmental delay and movement disorders has not been confirmed. In addition, ketogenic diet can lead to side effects including renal stones. In general, Glut1 DS patients are considered relatively refractory to antiepileptic drugs with only approximately 8% achieving seizure control on antiepileptic drugs alone. There are currently no antiepileptic drugs approved specifically for patients with Glut1 DS.

UX007 is intended as a substrate replacement therapy to provide an alternative source of energy to the brain in Glut1 DS patients. There are open-label investigator-sponsored clinical studies ongoing, and there is one publication presenting data on absence seizure reduction and improved developmental function in some Glut1 DS subjects taking UX007.

In March 2014, we initiated a Phase 2 global, randomized, double-blind, placebo-controlled, parallel-group clinical study that plans to enroll up to 40 patients who are currently not fully compliant with ketogenic diet and continue to have seizures. The primary efficacy objective is the reduction in frequency of seizures compared to placebo following a 6-week baseline period and subsequent 8-week placebo-controlled treatment period. Other efficacy objectives include cognitive function and movement disorder. The blinded treatment period will be followed by an open-label extension period in which patients will be treated with UX007 through week 52. In order to accelerate enrollment, we amended the enrollment criteria to also include patients with only absence seizures. Screening has been closed and we expect that up to 40 patients will be enrolled in the study. Data are expected in the second half of 2016.

In April 2015, positive data from an investigator-sponsored study of UX007 for the treatment of movement disorders associated with Glut1 DS were presented at the American Academy of Neurology Annual Meeting. The data showed a statistically significant 90% reduction in movement disorder events after treatment with UX007 (p=0.028) and a statistically significant increase in events after withdrawal from treatment with UX007 (p=0.043). Based on these study results, in November 2015 we announced an update to our development plan for UX007 in Glut1 DS patients. We now plan to initiate a Phase 3 study in approximately 40 Glut1 DS patients with the movement disorder phenotype in the second half of 2016. The study is intended to be a randomized, double-blind, placebo-controlled, double cross-over study. The study is designed to assess the impact of UX007 on movement disorder events as recorded by a patient diary. In recent interactions with the FDA, they have raised questions about the clinical meaningfulness of Glut1 DS movement disorder events. Therefore, we are working on further substantiating the clinical meaningfulness of Glut1 DS movement disorder events captured by a patient diary prior to finalizing the study design.

Ace-ER (UX001) for the treatment of GNE myopathy

We are developing Ace-ER, which is an extended-release, oral formulation of sialic acid for the treatment of GNE myopathy, which is also known as hereditary inclusion body myopathy, or HIBM. GNE myopathy is characterized by severe progressive muscular myopathy, or disease in which muscle fibers do not function properly, with onset typically in the late teens or twenties. Patients with GNE myopathy have a genetic defect in the gene coding for a particular enzyme that is involved in the first step in the biosynthesis of sialic acid. Therefore, GNE myopathy patients have a sialic acid deficiency, which interferes with muscle function, leading to myopathy and atrophy. Patients typically lose major muscle function within ten to 20 years of diagnosis. There is no approved drug therapy for GNE myopathy.

Ace-ER is intended as a potential substrate replacement therapy designed to address sialic acid deficiency and restore muscle function in GNE myopathy patients. We have conducted a Phase 2 randomized, double-blind, placebo-controlled study of Ace-ER in 47 GNE myopathy patients. Data from this study were presented at the American Academy of Neurology Annual Meeting in April 2014. Patients in the study were initially randomized to receive placebo, three grams, or six grams of Ace-ER per day. After 24 weeks, placebo patients crossed over to either three grams or six grams total daily dose, for an additional 24 weeks. The final analysis compared change at week 48 from baseline for the combined groups at six grams versus three grams of Ace-ER. Assessments included pharmacokinetics, composites of upper extremity and lower extremity muscle strength as measured by dynamometry, other clinical endpoints, patient reported outcomes, and safety.

At 24 weeks, assessments of upper extremity composite of muscle strength showed a statistically significant difference in the six-gram group compared to placebo (+2.33 kg; 5.5% relative difference from baseline; p=0.040). At 48 weeks, a statistically significant difference between the combined six-gram group and the combined three-gram group was observed (+3.44 kg; 8.5% relative difference from baseline; p=0.0033). Patients with less advanced disease (able to walk more than 200 meters at baseline), a predefined subset, showed a more pronounced difference (+4.69 kg; 9.6% relative difference from baseline; p=0.00055). The lower extremity composite showed a similar pattern of response but did not show a statistically significant difference between the dose groups. None of the groups showed a significant decline in the lower extremity composite during the treatment period. A positive trend was seen in patient-reported outcomes of functional activity consistent with the potential clinical meaningfulness of the muscle strength assessment. Ace-ER appeared to be well tolerated with no serious adverse events observed to date in either dose group, and no dose-dependent treatment-emergent adverse events were identified. Most adverse events were mild to moderate and the most commonly reported adverse events were gastrointestinal in nature and pain related to muscle biopsy procedures.

We continued to treat these patients in an extension study evaluating an increased daily dosage of sialic acid based on the dose dependence observed at weeks 24 and 48. Interim data from the extension study were presented at the International Congress of the World Muscle Society, or WMS, in October 2014. In the first part of the extension study, all 46 patients who completed the 48-week Phase 2 study crossed over to six grams for a variable period of time that was on average 24 weeks. In the second part of the extension study, all 46 patients and 13 treatment-naïve patients received 12 grams of Ace-ER for 24 weeks. The results presented at WMS included the 49 out of 59 patients who had 24 weeks of data at the higher dose. While the 12-gram data did not suggest any clinically meaningful advantage over six grams, the 12-gram data do provide additional data that supported clinical activity with Ace-ER treatment. The higher dose appeared to be generally safe and well tolerated with no drug-related serious adverse events, but the rate of mild to moderate gastrointestinal adverse events did appear to be greater with this dose. Throughout the approximately two-year study period, treatment with Ace-ER appeared to slow the progression of upper extremity disease when compared to the 24-week placebo group extrapolated out to two years.

We initiated a randomized, double-blind, placebo-controlled 48-week pivotal Phase 3 study of Ace-ER in 89 patients with GNE myopathy in May 2015 and completed enrollment in July 2016. The FDA agreed with the Phase 3 study design, including the primary endpoint of a composite of upper extremity muscle strength, with supportive secondary endpoint data from a patient-reported outcome, both of which were studied in the Phase 2 study. Data from the Phase 3 study are expected in 2017.

In October 2015 we announced the filing and acceptance for review of an MAA seeking conditional approval from the EMA based on our Phase 2 study results for the use of six grams per day of Ace-ER tablets in the treatment of GNE myopathy. The CHMP opinion on the conditional marketing authorization is expected in the second half of 2016 and a decision from the European Commission is expected in the first half of 2017.

Preclinical Pipeline

rhPPCA (UX004) for the treatment of galactosialidosis

Recombinant human protective protein cathepsin-A, or rhPPCA, which we in-licensed from St. Jude Children's Research Hospital in September 2012, is in preclinical development as an enzyme replacement therapy for galactosialidosis, a rare lysosomal storage disease for which there are no currently approved drug therapies. Similar to MPS patients, patients with galactosialidosis present with both soft tissue storage in the liver, spleen, and other tissues, as well as connective tissue (bone and cartilage) related disease. As with MPS 7, an enzyme deficiency results in accumulation of substrates in the lysosomes, causing skeletal and organ dysfunction, and death. We are continuing preclinical development of rhPPCA with plans to file an investigational new drug application, or IND, in 2017.

Collaboration with Arcturus Therapeutics, Inc. for mRNA therapeutics

We signed a research collaboration and license agreement with Arcturus Therapeutics, Inc. to develop mRNA therapeutics for select rare disease targets in October 2015. The Arcturus collaboration may help us address a wider range of rare diseases than possible with current approaches. As part of the collaboration, Arcturus will utilize its UNA Oligomer™ chemistry and LUNAR™ nanoparticle delivery platform to initially design and optimize mRNA therapeutics for two targets selected by us; we also have the option to add up to eight additional targets during the collaborative research period.

Collaboration with Takeda Pharmaceutical Company Limited

We entered into a strategic partnership with Takeda Pharmaceutical Company Limited to develop and commercialize therapies to treat rare genetic diseases in June 2016. As part of the collaboration, we will initially receive an exclusive license to one preclinical Takeda product candidate in a pre-determined field of use, and will have an exclusive option to co-develop and co-commercialize the product candidate in additional therapeutic areas. We have also established a five-year research collaboration with Takeda in which we will have the option to license up to five additional Takeda product candidates for rare diseases.

Other preclinical programs

We continue to work on other compounds in various preclinical stages of development.

Financial Operations Overview

We are a clinical-stage company and have only a limited operating history. To date, we have invested substantially all of our efforts and financial resources to identifying, acquiring, and developing our product candidates, including conducting clinical studies and providing general and administrative support for these operations. To date, we have funded our operations primarily from the sale of equity securities.

We have never been profitable and have incurred net losses in each year since inception. Our net losses were $56.9 million and $29.8 million for the three months ended June 30, 2016 and 2015, $109.7 million and $51.2 million for the six months ended June 30, 2016 and 2015, respectively. Substantially all of our net losses have resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations.

Revenue

We recorded revenue for UX003 in the second quarter of 2016 for named patient sales in Europe. All of the costs to manufacture the associated inventory were expensed as incurred because the product is not approved for commercial sale. We do not expect to receive any significant revenue until we obtain regulatory approval for any product candidates that we develop and commercialize them or enter into collaborative agreements with third parties through which we could generate revenue.

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for the development of our product candidates, which include:

- expenses incurred under agreements with clinical study sites that conduct research and development activities on our behalf;
- expenses incurred under license agreements with third parties;
- employee and consultant-related expenses, which include salaries, benefits, travel, and stock-based compensation;
- laboratory and vendor expenses related to the execution of preclinical, non-clinical, and clinical studies;
- the cost of acquiring, developing, and manufacturing clinical study materials; and
- facilities, depreciation, and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance, and other supply costs.

We expense all research and development costs in the periods in which they are incurred. Costs for certain development activities are recognized based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors and clinical sites. Nonrefundable advance payments for goods or services to be received in future periods for use in research and development activities are deferred and capitalized. The capitalized amounts are then expensed as the related goods are delivered and the services are performed.

The largest component of our total operating expenses has historically been our investment in research and development activities, including the clinical development of our product candidates. We allocate research and development salaries, benefits, stock-based compensation, and indirect costs to our product candidates on a program-specific basis, and we include these costs in the program-specific expenses. We expect our research and development expenses will increase in absolute dollars in future periods as we continue to invest in research and development activities related to developing our product candidates, and as programs advance into later stages of development and we enter into larger clinical studies. The process of conducting the necessary clinical research to obtain FDA approval is costly and time consuming and the successful development of our product candidates is highly uncertain. As a result, we are unable to determine the duration and completion costs of our research and development projects or when and to what extent, if any, we will generate revenue from the commercialization and sale of any of our product candidates.

General and Administrative Expenses

General and administrative expenses consist primarily of personnel costs, allocated facilities costs, and other expenses for outside professional services, including legal, human resources, audit, and accounting services. Personnel costs consist of salaries, benefits, and stock-based compensation. We expect that our general and administrative expenses will increase in the future to support continued research and development activities, preparation for potential commercialization of our product candidates, and as a result of operating as a public company, including expenses related to compliance with the rules and regulations of the Securities and Exchange Commission, or SEC, and those of any national securities exchange on which our securities are traded, additional insurance expenses, investor relations activities, and other administration and professional services.

Interest income

Interest income consists of interest earned on our cash, cash equivalents, and investments.

Other income (expense)

Other income (expense) primarily consists of foreign currency exchange gains and losses. Our foreign currency exchange gains and losses relate to transactions and asset and liability balances denominated in currencies other than the U.S. dollar.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our condensed consolidated financial statements, which have been prepared in accordance with GAAP. The preparation of these condensed consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. There have been no significant and material changes in our critical accounting policies during the six months ended June 30, 2016, as compared to those disclosed in "Management's Discussion and Analysis of Financial Condition and Results of Operations-Critical Accounting Policies and Significant Judgments and Estimates" in our in our most recent Annual Report on Form 10-K filed with the SEC.

Results of Operations

Comparison of the three months and six months ended June 30, 2016 to the three and six months ended June 30, 2015:

Revenue (dollars in thousands)

	Three Months Ended June 30,		Dollar	%
	2016	2015	Change	Change
Revenue	$ 17	$ -	$ 17	*

	Six Months Ended June 30,		Dollar	%
	2016	2015	Change	Change
Revenue	$ 17	$ -	$ 17	*

We recognized revenue for a nominal amount of named patient sales of UX003 in Europe for the three and six months ended June 30, 2016. We did not recognize any revenue for the three and six months ended June 30, 2015.

Research and Development Expenses (dollars in thousands)

	Three Months Ended June 30,		Dollar	%
	2016	2015	Change	Change
Development candidate:				
KRN23 (XLH)	$ 8,029	$ 2,333	$ 5,696	244%
KRN23 (TIO)	758	166	592	357%
rhGUS	7,010	5,179	1,831	35%
UX007 (LC-FAOD)	3,801	2,307	1,494	65%
UX007 (Glut 1 DS)	3,445	1,658	1,787	108%
Ace-ER	7,710	6,084	1,626	27%
Other research costs and preclinical costs	12,579	5,377	7,202	134%
Total research and development expenses	$ 43,332	$ 23,104	$ 20,228	88%

	Six Months Ended June 30,		Dollar	%
	2016	2015	Change	Change
Development candidate:				
KRN23 (XLH)	$ 14,483	$ 4,203	$ 10,280	245%
KRN23 (TIO)	1,047	361	686	190%
rhGUS	14,095	8,579	5,516	64%
UX007 (LC-FAOD)	9,857	4,773	5,084	107%
UX007 (Glut 1 DS)	6,508	3,292	3,216	98%
Ace-ER	15,507	10,595	4,912	46%
Other research and development costs	22,250	8,665	13,585	157%
Total research and development expenses	$ 83,747	$ 40,468	$ 43,279	107%

Research and development expenses increased $20.2 million and $43.3 million for the three months and six months ended June 30, 2016, compared to the same periods in 2015. The increase in research and development expenses shown above is primarily due to:

- for KRN23 (XLH), an increase of $5.7 million and $10.3 million for the three months and six months ended June 30, 2016, respectively, related to the continued development of our clinical program, the enrollment of our Phase 3 adult study, and other development planning and regulatory activities, net of KHK reimbursement;
- for KRN23 (TIO), an increase of $0.6 million and $0.7 million for the three months and six months ended June 30, 2016, respectively, related to the continued development of our adult TIO study and other development planning and regulatory activities, net of KHK reimbursement;
- for rhGUS, an increase of $1.8 million and $5.5 million for the three months and six months ended June 30, 2016, respectively, related to our Phase 3 clinical program and increases in manufacturing-related and quality activities;
- for UX007 (LC-FAOD), an increase of $1.5 million and $5.1 million for the three months and six months ended June 30, 2016, respectively, related to clinical manufacturing, the continued development of our clinical program, and support of investigator-sponsored studies across multiple diseases;
- for UX007 (Glut1 DS), an increase of $1.8 million and $3.2 million for the three months and six months ended June 30, 2016, respectively, related to the continued development of our clinical program, including patient identification;

- for Ace-ER, an increase of $1.6 million and $4.9 million for the three months and six months ended June 30, 2016, respectively, related to the enrollment of our Phase 3 study, and manufacturing, quality, and regulatory activities for this program; and
- an increase of $7.2 million and $13.6 million for the three months and six months ended June 30, 2016, respectively, in other research and development costs including expenses in support of our clinical product candidate pipeline, expenses related to our research stage programs and research collaborations, and certain cost allocations, including stock compensation.

We expect our research and development expenses to increase in the future as we advance our product candidates through clinical development. The timing and amount of expenses incurred will depend largely upon the outcomes of current or future clinical studies for our product candidates as well as the related regulatory requirements, manufacturing costs and any costs associated with the advancement of our preclinical programs.

General and Administrative Expenses (dollars in thousands)

	Three Months Ended June 30,		Dollar	%
	2016	2015	Change	Change
General and administrative	$ 14,738	$ 7,038	$ 7,700	109%

	Six Months Ended June 30,		Dollar	%
	2016	2015	Change	Change
General and administrative	$ 27,945	$ 11,176	$ 16,769	150%

General and administrative expenses increased $7.7 million and $16.8 million for the three months and six months ended June 30, 2016, respectively, compared to the same periods in 2015. The increase in general and administrative expenses was primarily due to increases in commercial planning costs, professional services costs, stock-based compensation, and personnel costs resulting from an increase in employees in support of our activities.

We expect general and administrative expenses to increase to support our organizational growth, the costs of being a public company, and for our expected staged build out of our commercial organization over the next several years related to multiple late-stage product candidates.

Interest Income (dollars in thousands)

	Three Months Ended June 30,		Dollar	%
	2016	2015	Change	Change
Interest income	$ 971	$ 456	$ 515	113%

	Six Months Ended June 30,		Dollar	%
	2016	2015	Change	Change
Interest income	$ 1,955	$ 729	$ 1,226	168%

Interest income increased $0.5 million and $1.2 million for the three months and six months ended June 30, 2016, respectively, compared to the same periods in 2015, primarily due to funds invested from our underwritten public offering in July 2015 and increased yield on our investment portfolio.

Other Income (Expense), net (dollars in thousands)

	Three Months Ended June 30,		Dollar	%
	2016	2015	Change	Change
Other income (expense), net	$ 159	$ (101)	$ 260	-257%

	Six Months Ended June 30,		Dollar	%
	2016	2015	Change	Change
Other income (expense), net	$ 40	$ (251)	$ 291	-116%

Other income (expense), net increased $0.3 million for the three months and six months ended June 30, 2016, compared to the same periods in 2015, primarily due to more favorable foreign exchange rates in the current year.

Liquidity and Capital Resources

Since our inception, we have funded our operations primarily with $103.9 million in net proceeds from the sale of convertible preferred stock, $121.7 million in net proceeds from the sale of common stock in our IPO and $521.4 million in net proceeds from the sale of common stock in our underwritten public offerings following our IPO. In July 2016, we entered into an At-The-Market, or ATM, sales agreement with Cowen under which we may offer and sell our common stock having aggregate proceeds of up to $150.0 million from time to time. In July 2016, we also consummated a common stock purchase agreement with Takeda whereby Takeda purchased 374,590 shares of the Company's common stock for total consideration of $40.0 million. Beginning three months after July 21, 2016, the effective date of the collaboration, we have an option, exercisable at our sole discretion, to require Takeda to purchase an additional $25.0 million in shares of common stock at the then-current 30-day VWAP, with such right expiring on the first anniversary of the effective date of the collaboration. Contingent upon meeting certain other milestones as noted in the collaboration agreement, we have a second option, exercisable in our sole discretion, to require Takeda to purchase an additional $10.0 million in shares of common stock at the then-current 30-day VWAP.

As of June 30, 2016, we had $441.8 million in available cash, cash equivalents, and investments. Our cash, cash equivalents, and investments are held in a variety of interest-bearing accounts, corporate debt securities, U.S. government securities, and money market accounts. Cash in excess of immediate requirements is invested with a view toward liquidity and capital preservation, and we seek to minimize the potential effects of concentration and credit risk.

The following table summarizes our cash flows for the periods indicated (in thousands):

	Six Months Ended June 30,	
	2016	2015
Cash used in operating activities	$ (84,550)	$ (34,932)
Cash provided by (used in) investing activities	45,761	(115,076)
Cash provided by financing activities	289	178,035
Net increase (decrease) in cash and cash equivalents	$ (38,500)	$ 28,027

Cash Used in Operating Activities

Our primary use of cash is to fund operating expenses, which consist primarily of research and development expenditures. Due to our significant research and development expenditures, we have generated significant operating losses since our inception. Cash used to fund operating expenses is affected by the timing of when we pay these expenses, as reflected in the change in our outstanding accounts payable and accrued expenses.

Cash used in operating activities for the six months ended June 30, 2016 was $84.6 million and reflected a net loss of $109.7 million, offset by non-cash charges of $1.2 million for depreciation and amortization, $3.2 million for the amortization of premium paid on purchased investments, and $21.1 million for stock-based compensation. Cash used in operating activities also reflected a $4.6 million increase in prepaid expenses and other current assets primarily due to an increase in deferred rent for the commencement of a new lease and increases in KHK receivable, prepaid manufacturing costs, and prepaid clinical costs. There was also a $0.9 million increase in other assets primarily due to an increase in prepaid clinical costs, a $2.8 million increase in accounts payable primarily due to higher collaboration and research costs, and a $2.2 million increase in accrued expenses and other liabilities as a result of increases in clinical study, manufacturing, and related costs as we continued to increase our research and development activities.

Cash used in operating activities for the six months ended June 30, 2015 was $34.9 million and reflected a net loss of $51.2 million, offset by non-cash charges of $0.5 million for depreciation and amortization, $2.2 million for the amortization of premium paid on purchased short-term investments, and $7.5 million for stock-based compensation. Cash used in operating activities also reflected a $3.5 million increase in prepaid expenses and other current assets primarily due to an increase in costs in contract research organization, CRO, other prepaid clinical costs, and prepaid insurance expenses, a $4.8 million increase in accounts payable primarily due to timing of payments, higher clinical study and related costs and an increase in professional fees, and a $4.8 million increase in accrued expenses and other liabilities as a result of an increase in clinical study, manufacturing, and related costs as we continued to increase our research and development activities offset by a decrease in employee bonuses.

Cash Provided by or Used in Investing Activities

Cash provided by investing activities for the six months ended June 30, 2016 was $45.8 million and related to purchases of investments of $223.1 million, purchases of property and equipment of $6.5 million and an increase of $1.5 million in restricted cash for the expansion of the space under our current lease agreement, offset by proceeds from maturities of investments of $222.6 million and the sale of investments of $54.3 million.

Cash used in investing activities for the six months ended June 30, 2015 was $115.1 million and related to purchases of short-term investments of $242.4 million, purchases of property and equipment of $1.1 million and an increase of $1.2 million in restricted cash for the expansion of the space under our current lease, offset by proceeds from maturities of short-term investments of $109.4 million and the sale of investments of $20.3 million.

Cash Flows Provided by Financing Activities

Cash provided by financing activities for the six months ended June 30, 2016 was $0.3 million and was comprised of proceeds from the issuance of common stock from the exercise of stock options.

Cash provided by financing activities for the six months ended June 30, 2015 was $178.0 million and was comprised of proceeds from the issuance of common stock from our underwritten public offering and the exercise of stock options and warrants.

Funding Requirements

We anticipate that we will continue to generate losses for the foreseeable future, and we expect the losses to increase as we continue the development of, and seek regulatory approvals for, our product candidates, and begin to commercialize any approved products. We will likely require additional capital to fund our operations and complete our ongoing and planned clinical studies, and funding may not be available to us on acceptable terms or at all. We expect to satisfy future cash needs through existing capital balances or, if necessary, through equity or debt financings, or strategic collaborations. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may be required to delay, limit, reduce the scope of, or terminate one or more of our clinical studies, research and development programs, future commercialization efforts, or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Our future funding requirements will depend on many factors, including the following:

- the scope, rate of progress, results and cost of our clinical studies, nonclinical testing, and other related activities;
- the cost of manufacturing clinical supplies, and establishing commercial supplies, of our product candidates and any products that we may develop;
- the number and characteristics of product candidates that we pursue;
- the cost, timing, and outcomes of regulatory approvals;
- the cost and timing of establishing commercial infrastructure, and distribution capabilities; and
- the terms and timing of any collaborative, licensing, and other arrangements that we may establish, including any required upfront milestone and royalty payments thereunder.

We may seek to raise any necessary additional capital through some combination of public or private equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements, and other marketing and distribution arrangements. To the extent that we raise additional capital through marketing and distribution arrangements or other collaborations and strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our product candidates, future revenue streams, research programs, or product candidates or grant licenses on terms that may not be favorable to us. If we do raise additional capital through public or private equity offerings, the ownership interest of our existing stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights. If we raise additional capital through debt financing, we may be subject to covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

Contractual Obligations and Commitments

During the six months ended June 30, 2016, there were no material changes to our contractual obligations and commitments described under Management's Discussion and Analysis of Financial Condition and Results of Operations in our Annual Report on Form 10-K for the year ended December 31, 2015.

Off-Balance Sheet Arrangements

Since our inception in April 2010, we have not engaged in any off-balance sheet arrangements, as defined in the rules and regulations of the SEC.

Item 3. ***Quantitative and Qualitative Disclosures About Market Risk***

Our exposure to market risk for changes in interest rates relates primarily to interest earned on our cash equivalents and investments. The primary objective of our investment activities is to preserve our capital to fund operations. A secondary objective is to maximize income from our investments without assuming significant risk. Our investment policy provides for investments in low-risk, investment-grade debt instruments. As of June 30, 2016, we had cash, cash equivalents, and investments totaling $441.8 million which includes bank deposits, money market funds, asset-backed securities, and investment-grade corporate bonds which are subject to default, changes in credit rating, and changes in market value. The securities in our investment portfolio are classified as available for sale and are subject to interest rate risk and will decrease in value if market interest rates increase. A hypothetical 100 basis point shift change in interest rates during any of the periods presented would not have had a material impact on our financial statements. To date, we have not experienced a loss of principal on any of our investments.

We face foreign exchange risk as a result of entering into transactions denominated in currencies other than U.S. dollars. Due to the uncertain timing of expected payments in foreign currencies, we do not utilize any forward exchange contracts. All foreign transactions settle on the applicable spot exchange basis at the time such payments are made. An adverse movement in foreign exchange rates could have a material effect on payments made to foreign suppliers and for license agreements. A hypothetical 10% change in foreign exchange rates during any of the periods presented would not have had a material impact on our financial statements.

Item 4. ***Controls and Procedures***

Evaluation of Disclosure Controls and Procedures

We carried out an evaluation, under the supervision and with the participation of our management, including our Chief Executive Officer and our Chief Financial Officer, of the effectiveness of our “disclosure controls and procedures” as of the end of the period covered by this report, pursuant to Rules 13a-15(b) and 15d-15(b) under the Exchange Act of 1934, as amended, or the Exchange Act. In connection with that evaluation, our Chief Executive Officer and our Chief Financial Officer concluded that our disclosure controls and procedures were effective and designed to provide reasonable assurance that the information required to be disclosed is recorded, processed, summarized, and reported within the time periods specified in the SEC rules and forms as of June 30, 2016. For the purpose of this review, disclosure controls and procedures means controls and procedures designed to ensure that information required to be disclosed by us in the reports that we file or submit is recorded, processed, summarized, and reported within the time periods specified in the SEC’s rules and forms. These disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by us in the reports that we file or submit is accumulated and communicated to management, including our principal executive officer and principal financial officer, as appropriate to allow timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, our management recognized that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives, and our management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Changes in Internal Control over Financial Reporting

During the quarter ended June 30, 2016, we completed the implementation of supply chain modules to our existing enterprise resource planning (ERP) system. In connection with several core financial and purchasing modules implemented in 2015, we have updated the processes that constitute our internal control over financial reporting, as necessary, to accommodate related changes to our business processes and accounting procedures. We will continue to build out our ERP system in a phased approach.

Except as otherwise described above, there have been no other changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during our second quarter ended June 30, 2016, that has materially affected, or is reasonably likely to materially affect our internal control over financial reporting.

PART II. OTHER INFORMATION

Item 1. *Legal Proceedings*

We are not currently a party to any material legal proceedings. We may, however, in the ordinary course of business face various claims brought by third parties and we may, from time to time, make claims or take legal actions to assert our rights, including intellectual property rights as well as claims relating to employment matters and the safety or efficacy of our products. Any of these claims could subject us to costly litigation and, while we generally believe that we have adequate insurance to cover many different types of liabilities, our insurance carriers may deny coverage, may be inadequately capitalized to pay on valid claims, or our policy limits may be inadequate to fully satisfy any damage awards or settlements. If this were to happen, the payment of any such awards could have a material adverse effect on our consolidated operations, cash flows, and financial position. Additionally, any such claims, whether or not successful, could damage our reputation and business.

Item 1A. *Risk Factors*

Investing in our common stock involves a high degree of risk. You should carefully consider the following risks, together with all the other information in this report, including our financial statements and notes thereto, before deciding to invest in our common stock. If any of the following risks actually materializes, our operating results, financial condition, and liquidity could be materially adversely affected. As a result, the trading price of our common stock could decline and you could lose part or all of your investment.

Risks Related to Our Financial Condition and Capital Requirements

We are a clinical-stage company and have a limited operating history on which to assess our business, have incurred significant losses since our inception, and anticipate that we will continue to incur significant losses for the foreseeable future.

We are a clinical-stage biopharmaceutical company with a limited operating history. We have incurred net losses in each year since our inception in April 2010, including net losses of $56.9 million and $29.8 million for the three months ended June 30, 2016 and 2015, and net losses of $109.7 million and $51.2 million for the six months ended June 30, 2016 and 2015, respectively.

We have devoted substantially all of our financial resources to identifying, acquiring, and developing our product candidates, including conducting clinical studies, developing manufacturing processes, manufacturing product candidates for clinical studies, and providing general and administrative support for these operations. To date, we have financed our operations primarily through the sale of equity securities. The amount of our future net losses will depend, in part, on the rate of our future expenditures and our ability to obtain funding through equity or debt financings, strategic collaborations, or grants. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. Our product candidates are in clinical development and we may never have a product candidate approved for commercialization, though UX003 is currently available on a named patient basis in certain countries in Europe. If we obtain regulatory approval to market a product candidate, our future revenue will depend upon the size of any markets in which our product candidates may receive approval, and our ability to achieve sufficient market acceptance, pricing, reimbursement, and adequate market share for our product candidates in those markets. However, even if we obtain adequate market share for our product candidates, because the potential markets in which our product candidates may ultimately receive regulatory approval are very small, and our expenses may be greater than expected, we may never become profitable despite obtaining such market share and acceptance of our products.

We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. We anticipate that our expenses will increase substantially if and as we:

- continue our research and nonclinical and clinical development of our product candidates;
- expand the scope of our current clinical studies for our product candidates;
- advance our programs into more expensive clinical studies;
- initiate additional nonclinical, clinical, or other studies for our product candidates;
- pursue preclinical and clinical development for additional indications for existing product candidates;
- change or add additional manufacturers or suppliers;
- seek regulatory and marketing approvals for our product candidates that successfully complete clinical studies;
- establish a marketing and distribution infrastructure and field force to commercialize any products for which we may obtain marketing approval;
- seek to identify, assess, license, acquire, and/or develop other product candidates, technologies, and/or businesses;
- make milestone or other payments under any license agreements;
- seek to maintain, protect, and expand our intellectual property portfolio;
- seek to attract and retain skilled personnel;

- create additional infrastructure, including facilities and systems, to support the growth of our operations, our product development, and our planned future commercialization efforts; and
- experience any delays or encounter issues with any of the above, including but not limited to failed studies, complex results, safety issues, inspection outcomes, or other regulatory challenges that require longer follow-up of existing studies, additional major studies, or additional supportive studies in order to pursue marketing approval.

Further, the net losses we incur may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance.

We have not generated any significant revenue from product sales and may never be profitable.

We have no products approved for commercialization and have not generated any significant revenue from product sales. Our ability to generate significant revenue and achieve profitability depends on our ability, alone or with strategic collaboration partners, to successfully complete the development of, and obtain the regulatory and marketing approvals necessary to commercialize one or more of our product candidates. We do not anticipate generating significant revenue from product sales in the near future. Our ability to generate substantial future revenue from product sales, including named patient sales, depends heavily on our success in many areas, including but not limited to:

- completing research and nonclinical and clinical development of our product candidates;
- obtaining regulatory and marketing approvals for product candidates for which we complete clinical studies;
- developing a sustainable and scalable manufacturing process for any approved product candidates and establishing and maintaining supply and manufacturing relationships with third parties that can conduct the processes and provide adequate (in amount and quality) product supply to support clinical development and the market demand for our product candidates, if approved;
- launching and commercializing product candidates for which we obtain regulatory and marketing approval, either directly or with a collaborator or distributor;
- obtaining market acceptance of our product candidates as viable treatment options;
- obtaining adequate reimbursement and pricing for our product candidates;
- our ability to sell our product candidates on a named patient basis or through an equivalent mechanism and the amount of revenue generated from such sales;
- addressing any competing technological and market developments;
- identifying, assessing, licensing, acquiring, and/or developing new product candidates, technologies, and/or businesses;
- negotiating favorable terms in any collaboration, licensing, or other arrangements into which we may enter;
- maintaining, protecting, and expanding our portfolio of intellectual property rights, including patents, trade secrets, and know-how; and
- attracting, hiring, and retaining qualified personnel.

Even if one or more of the product candidates that we develop is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. Our expenses could increase beyond expectations if we are required by the FDA, the EMA, or other regulatory agencies, domestic or foreign, to change our manufacturing processes or assays, or to perform clinical, nonclinical, or other types of studies in addition to those that we currently anticipate. In cases where we are successful in obtaining regulatory approvals to market one or more of our product candidates, our revenue will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval, the accepted price for the product, the ability to get reimbursement at any price, and whether we own the commercial rights for that territory. If the number of our addressable rare disease patients is not as significant as we estimate, the indication approved by regulatory authorities is narrower than we expect, or the reasonably accepted population for treatment is narrowed by competition, physician choice, or treatment guidelines, we may not generate significant revenue from sales of such products, even if approved. For example, the development of KRN23, rhGUS, and UX007 for pediatric use is an important part of our current business strategy; if we are unable to obtain regulatory approval for the desired age ranges, our business may suffer.

We will likely need to raise additional capital to fund our activities. This additional financing may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed may force us to delay, limit, or terminate our product development efforts or other activities.

We are currently advancing our KRN23, rhGUS, UX007, and Ace-ER product candidates through clinical development and our other product candidate, rhPPCA, as well as our other early stage research projects, through preclinical development. Developing our product candidates is expensive, and we expect our research and development expenses to increase substantially in connection with our ongoing activities, particularly as we advance our product candidates through clinical studies and potential global commercialization.

As of June 30, 2016, our available cash, cash equivalents, and investments were $441.8 million. We will likely require additional capital to obtain regulatory approval for, and to commercialize all of our product candidates. In addition, our operating plans may change as a result of many factors that may currently be unknown to us, and we may need to seek additional funds sooner than planned. Our future funding requirements will depend on many factors, including but not limited to:

- the scope, rate of progress, results, and cost of our clinical studies, nonclinical testing, and other related activities;
- the cost of manufacturing clinical supplies, and establishing commercial supplies, of our product candidates and any products that we may develop;
- the number and characteristics of product candidates that we pursue;
- the cost, timing, and outcomes of regulatory approvals;
- the cost and timing of establishing field forces, marketing, and distribution capabilities; and
- the terms and timing of any collaborative, licensing, acquisition, and other arrangements that we may establish, including any required milestone, royalty, and other payments thereunder.

Any additional fundraising efforts may divert our management's attention from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible securities would dilute all of our stockholders. The incurrence of indebtedness could result in increased fixed payment obligations and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell, or license intellectual property rights, and other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to seek funds through collaborative partnerships or other arrangements and we may be required to relinquish rights to some of our technologies or product candidates or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results, and prospects. Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or if we have specific strategic considerations.

If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay, or discontinue one or more of our research or development programs or the commercialization of any product candidates or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition, and results of operations.

Risks Related to the Discovery and Development of Our Product Candidates

We are heavily dependent on the success of our product candidates, some of which are in the early stages of clinical development, which is a lengthy and expensive process with uncertain outcomes and the potential for substantial delays. We cannot give any assurance that any of our product candidates will receive regulatory approval, which is necessary before they can be commercialized.

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical studies to demonstrate the safety and efficacy of the product candidates in humans. To date, we have invested substantially all of our efforts and financial resources to identifying, acquiring, and developing our product candidates, including conducting clinical studies and providing general and administrative support for these operations. We cannot be certain that any clinical studies will be conducted as planned or completed on schedule, if at all. Our inability to successfully complete nonclinical and clinical development could result in additional costs to us and negatively impact our ability to generate revenue. Our future success is dependent on our ability to successfully develop, obtain regulatory approval for, and then successfully commercialize our product candidates. We currently generate no significant revenue from sales of drugs, and we may never be able to develop or commercialize a marketable drug. We cannot be certain that any of our product candidates will be successful in clinical studies or receive regulatory approval. Further, our product candidates may not receive regulatory approval even if they are successful in some clinical studies. If we do not receive regulatory approvals for our product candidates, we may not be able to continue our operations.

Each of our product candidates is in development and will require additional clinical development, management of nonclinical, clinical, and manufacturing activities, regulatory approval, obtaining adequate manufacturing supply, building of a commercial organization, significant marketing efforts, and reimbursement before we generate any significant revenue from commercial product sales. We currently have multiple programs that are in clinical studies. Three of our product candidates have advanced into pivotal studies, but such studies may not result in approval. For Ace-ER, we filed for conditional marketing authorization in the EU on the basis of results from our Phase 2 study, which study was originally designed to serve as a hypothesis-generating exploratory study and not as a pivotal study. Additionally, the study had a small sample size, did not have a primary endpoint and had a pre-specified unblinding that occurred halfway during the treatment period. Accordingly, the data from this Phase 2 study are not as comprehensive or robust as data that are typically generated from a pivotal Phase 3 study. Although conditional marketing authorization initially allows for approval based on a positive benefit-risk assessment without providing comprehensive clinical data, marketing approval applications based on smaller and less definitive studies may entail a higher risk for rejection than the standard approval pathway. Additionally, our filing for conditional marketing authorization for Ace-ER represents our first application for regulatory approval of an investigational drug. In the course of interacting with the EMA on this filing, certain findings and observations have been made, including but not limited to safety and efficacy and deficiencies in our clinical and chemistry, manufacturing, and controls processes and procedures, which we are in the process of addressing. However, there can be no assurance that our responses to these issues will be adequate such that we will be able to secure approval with the current filing or within projected time periods. Even if we obtain conditional approval, it may be withdrawn under certain circumstances. In addition, confirmatory clinical studies would be required and could fail to demonstrate sufficient safety and efficacy to obtain full approval. We also currently plan to file for conditional marketing authorization for KRN23 for XLH in the EU based on Phase 1/2 and Phase 2 data. This filing would face similar hurdles.

Some of our product candidates are in the early-stage translational research phases of development. Such early-stage programs will require substantial investment to reach clinical studies and regulatory approval, and the risk of failure for them may be higher than with our clinical-stage product candidates. For example, our collaboration with Arcturus focuses on an advanced but less established technology platform that will require significant effort and investment. A failure in that collaboration or our other early-stage programs may negatively affect our operational results.

We generally plan to seek regulatory approval to commercialize our product candidates in the United States, the EU, and in additional foreign countries where we have commercial rights. To obtain regulatory approval in other countries, we must comply with numerous and varying regulatory requirements of such other countries regarding safety, efficacy, chemistry, manufacturing, and controls, clinical studies, commercial sales, pricing, and distribution of our product candidates. Even if we are successful in obtaining approval in one jurisdiction, we cannot ensure that we will obtain approval in any other jurisdictions. If we are unable to obtain approval for our product candidates in multiple jurisdictions, our revenue and results of operations could be negatively affected.

We cannot be certain that any of our product candidates will be successful in clinical studies or receive regulatory approval. Further, our product candidates may not receive regulatory approval even if they are successful in clinical studies. If we do not receive regulatory approvals for our product candidates, we may not be able to continue our operations.

The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time consuming, and inherently unpredictable. Even if we achieve positive results in our pre-clinical and clinical studies, if we are ultimately unable to obtain timely regulatory approval for our product candidates, our business will be substantially harmed.

Our future success is dependent on our ability to successfully develop, obtain regulatory approval for, and then successfully commercialize one or more product candidates. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from the FDA or comparable foreign regulatory authorities, and we may never receive such regulatory approval for any of our product candidates. We have not obtained regulatory approval for any product candidate, and it is possible that none of our existing product candidates or any product candidates we may seek to develop in the future will ever obtain regulatory approval.

To obtain regulatory approval in the United States and other jurisdictions, we must comply with numerous and varying requirements regarding safety, efficacy, chemistry, manufacturing and controls, clinical studies (including good clinical practices), commercial sales, pricing, and distribution of our product candidates. Even if we are successful in obtaining approval in one jurisdiction, we cannot ensure that we will obtain approval in any other jurisdictions. In addition, approval policies, regulations, positions of the regulatory agencies on study design and/or endpoints, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate’s clinical development, which may cause delays in the approval or the decision not to approve an application. Communications with the regulatory agencies during the approval process are also unpredictable; favorable communications early in the process do not ensure that approval will be obtained and unfavorable communications early on do not guarantee that approval will not be obtained. If we are unable to obtain approval for our product candidates in multiple jurisdictions, our revenue and results of operations could be negatively affected. Applications for our product candidates could fail to receive regulatory approval, or could be delayed in receiving regulatory approval, for many reasons, including but not limited to the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design, implementation, or conduct of our clinical studies;
- the FDA or other comparable foreign regulatory authorities may change their guidance or requirements for a development program for a product candidate;
- the population studied in the clinical program may not be sufficiently broad or representative to assure efficacy and safety in the full population for which we seek approval;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from nonclinical studies or clinical studies;
- the data collected from clinical studies of our product candidates may not be sufficient to support the submission of an NDA, or biologics license application, or BLA, or other submission or to obtain regulatory approval in the United States or elsewhere;
- we may be unable to demonstrate to the FDA or comparable foreign regulatory authorities that a product candidate's risk-benefit ratio for its proposed indication is acceptable;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes, test procedures and specifications, or facilities of third-party manufacturers with which we contract for clinical and commercial supplies;
- as a condition of marketing authorization in the EU, an agreed upon Pediatric Investigational Plan (PIP) detailing the designs and completion timelines for nonclinical and clinical studies is required. If the nonclinical or clinical development does not comply with the agreed upon PIP, marketing authorization could be denied or significantly delayed; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

Furthermore, the disease states we are evaluating often will not have clear regulatory paths for approval and/or do not have validated outcome measures. In these circumstances, we work closely with the regulatory authorities to define the approval path and may have to qualify outcome measures as part of our development programs. For example, for patients with XLH there is no available regulatory precedent for what is needed to obtain approval to treat this disease and there are no validated patient-reported outcome measures that are specific to this disease. Additionally, many of the disease states we are targeting are highly heterogeneous in nature, which may impact our ability to determine the treatment benefit of our potential therapies. For example, patients with FAOD, Glut1 DS, and MPS 7 have a highly heterogeneous disease course, which may impact our ability to determine the true treatment benefit of our product candidates in these patients.

This lengthy and uncertain approval process, as well as the unpredictability of the clinical and nonclinical studies, may result in our failing to obtain regulatory approval to market any of our product candidates, or being delayed in obtaining regulatory approval, which would significantly harm our business, results of operations, and prospects.

Clinical drug development involves a lengthy and expensive process with uncertain outcomes and the potential for substantial delays, and the results of earlier studies may not be predictive of future study results.

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical studies to demonstrate the safety and efficacy of the product candidates in humans. Clinical testing is expensive, time consuming, and uncertain as to outcome. We cannot guarantee that any clinical studies will be conducted as planned or completed on schedule, if at all. A failure of one or more clinical studies can occur at any stage of testing, and our future clinical studies may not be successful. Product candidates that have shown promising results in early-stage clinical studies may still suffer significant setbacks in subsequent clinical studies. For example, the safety or efficacy results generated to date in clinical studies for KRN23, rhGUS, UX007, and Ace-ER do not ensure that later clinical studies will demonstrate similar results. Results from investigator-sponsored studies or compassionate-use studies may not be confirmed in company-sponsored studies or may negatively impact the prospects for our programs. Additionally, given the nature of the rare diseases we are seeking to treat, we often have to devise newly-defined endpoints to be tested in our studies, which can lead to some subjectivity in interpreting study results and could result in regulatory agencies not agreeing with the validity of our endpoints, or our interpretation of the clinical data, and therefore denying approval. For example, for our Glut1 DS Phase 3 clinical trial, we have proposed utilizing a patient diary to track movement disorder events. Based on FDA feedback expressing concern about the clinical meaningfulness of all such events tracked, we are collecting additional supportive data on the clinical impact of events from patients and optimizing the diary in order to capture clinically meaningfulness of events. There is no guarantee that these modifications to the endpoint will be acceptable to FDA. Given the illness of the subjects in our studies and the nature of their rare diseases, we may also be required or choose to conduct certain studies on an open-label basis. Additionally, we have in the past, and may in the future elect to review interim clinical data at multiple time points during the studies, which could introduce bias into the study results and potentially result in denial of approval.

In the biopharmaceutical industry, there is a high failure rate for drugs and biologics proceeding through clinical studies, and product candidates in later stages of clinical studies may fail to show the desired safety and efficacy despite having progressed through nonclinical studies and initial clinical studies. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical studies due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier studies.

Scenarios that may prevent successful or timely completion of clinical development include but are not limited to:

- our inability to generate sufficient preclinical, toxicology, or other *in vivo* or *in vitro* data to support the initiation or continuation of human clinical studies or filings for regulatory approval;
- delays or failures in reaching a consensus with regulatory agencies on study design;
- delays in reaching agreement on acceptable terms with CROs, clinical study sites, and other clinical trial-related vendors;
- delays in obtaining required Institutional Review Board, or IRB, approval at each clinical study site;
- changes in clinical study design or development strategy resulting in delays related to obtaining approvals from IRBs and/or regulatory agencies to proceed with clinical studies;
- failure to gain approval from regulatory authorities or IRBs to conduct clinical studies in certain countries;
- imposition of a clinical hold by regulatory agencies after review of an IND application or amendment, another equivalent application or amendment, or an inspection of our clinical study operations or study sites;
- delays in recruiting suitable patients to participate in our clinical studies;
- difficulty collaborating with patient groups and investigators;
- failure by our CROs, other third parties, or us to adhere to clinical study requirements;
- failure to perform in accordance with the FDA's good clinical practices requirements or applicable regulatory guidelines in other countries;
- delays in patients' completion of studies or their returns for post-treatment follow-up;
- patients dropping out of a study;
- occurrence of adverse events associated with the product candidate that are viewed to outweigh its potential benefits;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;
- the cost of clinical studies of our drug candidates being greater than we anticipate;
- clinical studies of our drug candidates producing negative or inconclusive results, which may result in us deciding, or regulators requiring us, to conduct additional clinical or nonclinical studies or to abandon drug development programs;
- competing clinical studies of potential alternative product candidates or investigator-sponsored studies of our product candidates; and
- delays in manufacturing, testing, releasing, validating, or importing/exporting sufficient stable quantities of our product candidates for use in clinical studies or the inability to do any of the foregoing.

Any inability to successfully complete nonclinical and clinical development could result in additional costs to us or negatively impact our ability to generate revenue. In addition, if we make manufacturing or formulation changes to our product candidates, such as our plan to manufacture a combination extended release and immediate release version of sialic acid, or new formulations of UX007, we may need to conduct additional studies to bridge our modified product candidates to earlier approved versions. Clinical study delays could also shorten any periods during which our products have patent protection and may allow our competitors to bring products to market before we do, which could negatively impact our ability to obtain orphan exclusivity and to successfully commercialize our product candidates and may harm our business and results of operations.

We may find it difficult to enroll patients in our clinical studies given the limited number of patients who have the diseases for which our product candidates are being studied. Difficulty in enrolling patients could delay or prevent clinical studies of our product candidates.

Identifying and qualifying patients to participate in clinical studies of our product candidates is critical to our success. The timing of our clinical studies depends in part on the speed at which we can recruit patients to participate in testing our product candidates, and we may experience delays in our clinical studies if we encounter difficulties in enrollment.

Each of the conditions for which we plan to evaluate our current product candidates is a rare genetic disease. Accordingly, there are limited patient pools from which to draw for clinical studies. For our current product candidates:

- we estimate that several thousand patients in the United States suffer from XLH, for which KRN23 is being studied;
- we estimate that several hundred patients in the United States suffer from TIO, for which KRN23 is being studied;

- we estimate that up to approximately 200 patients in the developed world may suffer from MPS 7, for which rhGUS is being studied;
- we estimate that several thousand patients in the United States suffer from LC-FAOD, for which UX007 is being studied;
- we estimate that several thousand patients in the United States suffer from Glut1 DS, for which UX007 is being studied; and
- we estimate that approximately 2,000 patients in the developed world suffer from GNE myopathy, for which Ace-ER is being studied.

In addition to the rarity of these diseases, the eligibility criteria of our clinical studies will further limit the pool of available study participants as we will require that patients have specific characteristics that we can measure or to assure their disease is either severe enough or not too advanced to include them in a study. For example, the UX007 Glut1 DS Phase 2 study requires a certain minimum baseline rate of generalized tonic-clonic seizures or the presence of absence seizures at baseline. Additionally, the process of finding and diagnosing patients may prove costly. We also may not be able to identify, recruit, and enroll a sufficient number of patients to complete our clinical studies because of the perceived risks and benefits of the product candidate under study, the proximity and availability of clinical study sites for prospective patients, and the patient referral practices of physicians. The availability and efficacy of competing therapies and clinical studies can also adversely impact enrollment. For example, our Phase 2 UX007 Glut1 DS study is enrolling patients who are not currently on or compliant with the ketogenic diet. However, the ketogenic diet is the standard of care and considered effective in seizure control. If patients are unwilling to participate in our studies for any reason, the timeline for recruiting patients, conducting studies, and obtaining regulatory approval of potential products may be delayed, the commercial prospects of our product candidates will be harmed, and our ability to generate product revenue from any of these product candidates could be delayed or prevented. In addition, any delays in completing our clinical studies will increase our costs, slow down our product candidate development and approval process, and jeopardize our ability to commence product sales and generate revenue. Any of these occurrences may harm our business, financial condition, and prospects significantly. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical studies may also ultimately lead to the denial of regulatory approval of our product candidates.

If we do not achieve our projected development goals in the timeframes we announce and expect, the commercialization of our products may be delayed and the credibility of our management may be adversely affected and, as a result, our stock price may decline.

For planning purposes, we estimate the timing of the accomplishment of various scientific, clinical, regulatory, and other product development goals, which we sometimes refer to as milestones. These milestones may include the commencement or completion of scientific studies and clinical trials, the submission of regulatory filings, and the potential approval of such regulatory filings. We periodically make public announcements about the expected timing of some of these milestones. All of these milestones are based on a variety of assumptions, but the actual timing of these milestones can vary dramatically compared to our estimates, in many cases for reasons beyond our control. If we do not meet these milestones as publicly announced, the commercialization of our products may be delayed and the credibility of our management may be adversely affected and, as a result, our stock price may decline.

Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.

Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay, or halt clinical studies or further development, and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign authorities. Some of our product candidates are in the early stages of development and the safety profile has not been established. For example, in the completed Phase 1 study, four-month Phase 1/2 study, and long-term twelve-month Phase 1/2 study, adult patients treated with KRN23 have experienced drug-related side effects including injection site reaction, arthralgia, diarrhea, restless legs syndrome, injection site erythema, injection site pain, upper abdominal pain, headache, and decreased neutrophil count. Most of these adverse events were mild and no treatment-related serious adverse events have been observed. In interim Phase 2 data in pediatric patients, the most common treatment-related adverse event by preferred term was injection site reaction. There were no deaths and there was one serious adverse event of fever and muscle pain in a patient that was considered possibly treatment-related. Patients treated with triheptanoin have experienced drug-related side effects such as cramping, diarrhea, and loose stools. In addition, over 14 years of treatment experience in approximately 130 human subjects, including greater than 60 with LC-FAOD, we are aware of three serious adverse events that were classified as possibly related to triheptanoin treatment (muscle cell rupture and elevated creatine kinase reported for two subjects and myoglobinuria in one subject); however, these serious adverse events can be considered typical of the underlying disease. In interim data from our Phase 2 study, there were no deaths but there was one treatment-related serious adverse event of moderate gastroenteritis with vomiting. The most common treatment-related adverse events were diarrhea, abdominal/gastrointestinal pain, and vomiting. While we have not completed our own clinical studies for UX007, there may be other side effects associated with its use that we discover. Additionally, patients treated with Ace-ER have experienced drug-related side effects including mild gastrointestinal discomfort. Enzyme replacement therapies have been associated with infusion-associated reactions due to a developing allergy to the product, which can cause rashes, pain, significant clinical disease, or even death. Our rhGUS and rhPPCA product candidates may also cause these or similar side effects as further development proceeds. Results of our studies or investigator-sponsored trials could reveal a high and unacceptable severity and prevalence of these or other side effects. In such an event, our studies could be suspended or terminated, and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny or withdraw approval of our product candidates for any or all targeted indications.

Drug-related side effects could affect patient recruitment and the ability of enrolled patients to complete the study. Such side effects could also result in potential product liability claims. We currently carry product liability insurance in the amount of $10.0 million per incident and $10.0 million in the aggregate, and we are required to maintain product liability insurance pursuant to certain of our agreements. We believe our product liability insurance coverage is sufficient in light of our current clinical programs; however, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability, or losses may exceed the amount of insurance that we carry. A product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business. In addition, regardless of merit or eventual outcome, product liability claims may result in impairment of our business reputation, withdrawal of clinical study participants, costs due to related litigation, distraction of management's attention from our primary business, initiation of investigations by regulators, substantial monetary awards to patients or other claimants, the inability to commercialize our product candidates, and decreased demand for our product candidates, if approved for commercial sale.

Additionally, if our product candidates receive marketing approval, and we or others later identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including but not limited to:

- regulatory authorities may withdraw approvals of such product;
- regulatory authorities may require additional warnings on the product's label or restrict the product's approved use;
- we may be required to create a Risk Evaluation and Mitigation Strategy, or REMS, plan, which could include a medication guide outlining the risks of such side effects for distribution to patients, restricted distribution, a communication plan for healthcare providers, and/or other elements to assure safe use;
- we could be sued and held liable for harm caused to patients;
- patients and physicians may elect not to use our products, or reimbursement authorities may elect not to reimburse for them; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could significantly harm our business, results of operations, and prospects.

Even if we obtain regulatory approval for our product candidates, our products will remain subject to regulatory scrutiny.

If our product candidates are approved, they will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, distribution, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies, and submission of safety, efficacy, and other post-market information, including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities.

Manufacturers and manufacturers' facilities are required to comply with extensive FDA, and comparable foreign regulatory authority, requirements, including ensuring that quality control and manufacturing procedures conform to Good Manufacturing Practices (GMP) regulations. As such, we and our contract manufacturers will be subject to continual review and inspection to assess compliance with GMP and adherence to commitments made in any NDA, BLA, MAA, or other comparable application for approval in another jurisdiction. Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, and quality control.

Any regulatory approvals that we receive for our product candidates may be subject to limitations on the approved indicated uses for which the product may be marketed or other conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase IV clinical studies, and surveillance to monitor the safety and efficacy of the product candidate. We could also be asked to conduct post-marketing clinical studies to verify the safety and efficacy of our products in general or in specific patient subsets. If original marketing approval were obtained via the accelerated approval or conditional marketing authorization pathways, we would be required to conduct a successful post-marketing clinical study to confirm clinical benefit for our products. An unsuccessful post-marketing study or failure to complete such a study could result in the withdrawal of marketing approval. We will be required to report certain adverse events and manufacturing problems, if any, to the FDA and comparable foreign regulatory authorities. Any new legislation addressing drug safety issues could result in delays in product development or commercialization, or increased costs to assure compliance. We will have to comply with requirements concerning advertising and promotion for our products. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved label. As such, we may not promote our products for indications or uses for which they do not have approval. The holder of an approved NDA, BLA, MAA, or other comparable application must submit new or supplemental applications and obtain approval for certain changes to the approved product, product labeling, or manufacturing process.

If we fail to comply with applicable regulatory requirements, or there are safety or efficacy problems with a product, a regulatory agency or enforcement authority may, among other things:

- issue warning or notice of violation letters;
- impose civil or criminal penalties;
- suspend or withdraw regulatory approval;
- suspend any of our ongoing clinical studies;
- refuse to approve pending applications or supplements to approved applications submitted by us;
- impose restrictions on our operations, including closing our contract manufacturers' facilities;
- seize or detain products, or require a product recall; or
- require entry into a consent decree.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response, and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenue from our products. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our company and our operating results will be adversely affected.

Changes in methods of treatment of disease could reduce demand for our products and adversely affect revenues.

Even if our drug products are approved, if doctors elect a course of treatment which does not include our drug products, this decision would reduce demand for our drug products and adversely affect revenues. Changes in treatment method can be caused by the introduction of other companies' products or the development of new technologies or surgical procedures which may not directly compete with ours, but which have the effect of changing how doctors decide to treat a disease.

Risks Related to our Reliance on Third Parties

We rely on third parties to conduct our nonclinical and clinical studies and perform other tasks for us. If these third parties do not successfully carry out their contractual duties, meet expected deadlines, or comply with regulatory requirements, we may be exposed to sub-optimal quality and reputational harm, we may not be able to obtain regulatory approval for or commercialize our product candidates, and our business could be substantially harmed.

We have relied upon and plan to continue to rely upon third parties, including CROs and collaborative partners, to analyze, collect, monitor, and manage data for our ongoing nonclinical and clinical programs. We rely on third parties for execution of our nonclinical and clinical studies, and for estimates regarding costs and efforts completed, and we control only certain aspects of their activities. For example, we will rely on our partner Arcturus for the design and optimization of initial product candidates under our messenger RNA collaboration. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory, and scientific standards, and our reliance on the CROs and other third parties does not relieve us of our regulatory responsibilities. We and our CROs and other vendors and partners are required to comply with GMP, Good Clinical Practices (GCP), and Good Laboratory Practices (GLP), which are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area, and comparable foreign regulatory authorities for all of our product candidates in development. Regulatory authorities enforce these regulations through periodic inspections of study sponsors, principal investigators, study sites, and other contractors. If we or any of our CROs or other vendors and partners, including the sites at which clinical studies are conducted, fail to comply with applicable regulations, the data generated in our nonclinical and clinical studies may be deemed unreliable and the FDA, EMA, or comparable foreign regulatory authorities may deny approval and/or require us to perform additional nonclinical and clinical studies before approving our marketing applications, which would delay the approval process. We cannot make assurances that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical studies comply with GCP regulations or that nonclinical studies comply with GLP regulations. In addition, our clinical studies must be conducted with products produced under GMP regulations. If the regulatory authorities determine that we have failed to comply with GLP, GMP, or GCP regulations, they may deny approval of our product candidates and/or we may be required to repeat clinical or nonclinical studies, which would delay the regulatory approval process.

Our CROs and other vendors and partners are not our employees, and except for remedies available to us under our agreements with such third parties, we cannot control whether or not they devote sufficient time and resources to our on-going nonclinical and clinical programs. If our vendors and partners do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced, or if the quality or accuracy of the data they obtain is compromised due to the failure to adhere to our protocols, regulatory requirements, or for other reasons, our clinical studies may be extended, delayed, or terminated, and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. CROs and other vendors and partners may also generate higher costs than anticipated as a result of changes in scope of work or otherwise. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase, and our ability to generate revenue could be delayed.

If any of our relationships with these third parties terminate, we may not be able to enter into arrangements with alternative vendors or do so on commercially reasonable terms. Switching or adding additional vendors involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new vendor commences work. As a result, delays may occur, which can materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our vendors and partners, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition, and business prospects.

We also rely on third parties in other ways, including to support our patient identification efforts, to assist our finance and legal departments, and to provide other resources for our business. Use of these third parties could expose us to sub-optimal quality, missed deadlines, and non-compliance with applicable laws, all of which could result in reputational harm to us and negatively affect our business.

We are dependent on KHK for the clinical and commercial supply of KRN23 for all major markets and for the development and commercialization of KRN23 in certain major markets, and KHK's failure to provide an adequate supply of KRN23 or to commercialize KRN23 in those markets could result in a material adverse effect on our business and operating results.

Under our agreement with KHK, KHK has the sole right to commercialize KRN23 in Europe and, at a specified time, in the United States and Canada subject to a limited promotion right we retained. Our development partnership with KHK may not be successful, and we may not realize the expected benefits from such partnership, due to a number of important factors, including but not limited to the following:

- KHK has no obligation under our agreement to use diligent efforts to commercialize KRN23 in Europe. The timing and amount of any royalty payments we may receive under our agreement will depend on, among other things, the efforts, allocation of resources, and successful commercialization of KRN23 by KHK in Europe. Additionally, if KHK were to decide not to commercialize KRN23 in Europe, and we nevertheless wished to commercialize KRN23 in Europe, we would need to renegotiate with KHK certain terms of our agreement, which we may be unable to do on reasonable terms in a timely manner, or at all;
- the timing and amount of any royalty payments we may receive under our agreement with KHK will depend on, among other things, the efforts, allocation of resources, and successful commercialization of KRN23 by KHK in the United States and Canada under our agreement;
- KHK may change the focus of its commercialization efforts or pursue higher-priority programs;
- KHK may fail to manufacture or supply sufficient drug product of KRN23 in compliance with applicable laws and regulations or otherwise for our development and clinical use, which could result in program delays;
- KHK may fail to manufacture or supply sufficient drug product of KRN23 in compliance with applicable laws and regulations or otherwise for our commercial use, if approved, which could result in lost revenue;
- KHK may elect to develop and commercialize KRN23 indications with a larger market than XLH and at a lower price, thereby reducing the profit margin on sales of KRN23 for any orphan indications, including XLH;
- if KHK were to breach or terminate the agreement with us, we would no longer have any rights to develop or commercialize KRN23 or such rights would be limited to non-terminated countries;
- KHK may terminate its agreement with us, adversely affecting our potential revenue from licensed products; and
- the timing and amounts of expense reimbursement that we may receive are uncertain, and the total expenses for which we are obligated to reimburse KHK may be greater than anticipated.

We rely completely on third parties to manufacture our product candidates. Our business could be harmed if those third parties fail to provide us with sufficient quantities of drug product, or fail to do so at acceptable quality levels or prices.

We do not currently have, nor do we plan to acquire, the infrastructure or capability internally to manufacture our product candidates, and we lack the resources and the capability to manufacture any of our product candidates on a clinical or commercial scale. We rely on our manufacturers to purchase from third-party suppliers the materials necessary to produce our product candidates for our clinical studies. There are a limited number of suppliers for raw materials that we use to manufacture our drugs, placebos, or active controls, and there may be a need to identify alternate suppliers to prevent a possible disruption of the manufacture of the materials necessary to produce our product candidates for our clinical studies, and, if approved, ultimately for commercial sale. We do not have any control over the process or timing of the acquisition of these raw materials by our manufacturers. Although we generally do not begin a clinical study unless we believe we have a sufficient supply of a product candidate to complete such study, any significant delay or discontinuity in the supply of a product candidate, or the raw material components thereof, for an ongoing clinical study due to, among other things, the failure of a manufacturer to provide drug substance or drug product of sufficient quantity or quality, or the need to replace a third-party manufacturer could considerably delay completion of our clinical studies, product testing, and potential regulatory approval of our product candidates, and could also impair named patient sale supply of our product candidates, which could harm our business and results of operations.

We are subject to a multitude of manufacturing risks, any of which could substantially increase our costs and limit supply of our product candidates.

The process of manufacturing our product candidates is complex, highly regulated, and subject to several risks, including but not limited to:

- the process of manufacturing our product candidates is extremely susceptible to product loss due to contamination, equipment failure or improper installation or operation of equipment, or vendor or operator error. Even minor deviations from normal manufacturing processes for any of our product candidates could result in reduced production yields, product defects, and other supply disruptions. If microbial, viral, or other contaminations are discovered in our product candidates or in the manufacturing facilities in which our product candidates are made, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination; and
- the manufacturing facilities in which our product candidates are made could be adversely affected by equipment failures, labor shortages, raw material shortages, natural disasters, power failures, and numerous other factors.

Any adverse developments affecting manufacturing operations for our product candidates may result in shipment delays, inventory shortages, lot failures, withdrawals or recalls, or other interruptions in the supply of our product candidates. Due to their stage of development, small volume requirements, and infrequency of batch production runs, we carry limited amounts of safety stock for our product candidates. We may also have to take inventory write-offs and incur other charges and expenses for product candidates that fail to meet specifications, undertake costly remediation efforts, or seek more costly manufacturing alternatives.

The drug substance and drug product for most of our product candidates are currently acquired from single-source suppliers. The loss of these suppliers, or their failure to supply us with the necessary drug substance or drug product, could materially and adversely affect our business.

The drug substance and drug product for KRN23 are made by KHK pursuant to our license and collaboration agreement with KHK. The drug substance and drug product for rhGUS are manufactured by Rentschler Biotechnologie GmbH under a development and clinical supply agreement and accompanying purchase orders. The pharmaceutical-grade drug substance for UX007 is manufactured by IOI Oleo GmbH, or IOI Oleo, formerly Cremer Oleo GmbH & Co. KG, , pursuant to our supply agreement with IOI Oleo, and the drug product for UX007 is prepared by Haupt Pharma AG and CPM pursuant to purchase orders. The drug substance for Ace-ER is manufactured by Sanyo Fine Co., Ltd. under our license agreement and accompanying purchase orders with Nobelpharma Co., Ltd. and under our clinical supply agreement with Evonik Corporation, and the drug product for Ace-ER is manufactured by Alcami Corporation, or Alcami (formerly known as AAIPharma Services Corp., or AAIPharma), pursuant to our license agreement and accompanying purchase orders with Alcami. We have not currently secured any other suppliers for the drug substance or drug product of our product candidates and, although we believe that there are alternate sources of supply that could satisfy our clinical and commercial requirements, we cannot provide assurance that identifying alternate sources and establishing relationships with such sources would not result in significant delay in the development of our product candidates. Additionally, we may not be able to enter into supply arrangements with alternative suppliers on commercially reasonable terms or at all. A delay in the development of our product candidates or having to enter into a new agreement with a different third-party on less favorable terms than we have with our current suppliers could have a material adverse impact upon on our business.

We and our collaborators and contract manufacturers are subject to significant regulation with respect to manufacturing our product candidates. The manufacturing facilities on which we rely may not continue to meet regulatory requirements or may not be able to meet supply demands.

All entities involved in the preparation of therapeutics for clinical studies or commercial sale, including our existing contract manufacturers for our product candidates, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in clinical studies must be manufactured in accordance with GMP. These regulations govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of contaminants or to inadvertent changes in the properties or stability of our product candidates that may not be detectable in final product testing. We, our collaborators, or our contract manufacturers must supply all necessary documentation in support of an NDA, BLA, MAA, or other application for regulatory approval, on a timely basis and must adhere to GLP, GMP, and similar regulations enforced by the FDA and other regulatory agencies through their facilities inspection programs. Some of our contract manufacturers have never produced a commercially approved pharmaceutical product and therefore have not obtained the requisite regulatory authority approvals to do so. The facilities and quality systems of some or all of our collaborators and third-party contractors must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of our product candidates or any of our other potential products. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of our product candidates or our other potential products or the associated quality systems for compliance with the regulations applicable to the activities being conducted. Although we oversee the contract manufacturers, we cannot control the manufacturing process of, and are substantially dependent on, our contract manufacturing partners for compliance with the regulatory requirements. If these facilities do not pass a pre-approval plant inspection, regulatory approval of the products may not be granted or may be substantially delayed until any violations are corrected to the satisfaction of the regulatory authority, if ever.

The regulatory authorities also may, at any time following approval of a product for sale, audit the manufacturing facilities of our collaborators and third-party contractors. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly and/or time consuming for us or a third-party to implement, and that may include the temporary or permanent suspension of a clinical study or commercial sales or the temporary or permanent closure of a facility. Any such remedial measures imposed upon us or third parties with whom we contract could materially harm our business.

If we, our collaborators, or any of our third-party manufacturers fail to maintain regulatory compliance, the FDA or other applicable regulatory authority can impose regulatory sanctions including, among other things, refusal to approve a pending application for a new drug product or biologic product, withdrawal of an approval, or suspension of production. As a result, our business, financial condition, and results of operations may be materially harmed.

Additionally, if supply from one approved manufacturer is interrupted, an alternative manufacturer would need to be qualified through an NDA or BLA supplement or MAA variation, or equivalent foreign regulatory filing, which could result in further delay. The regulatory agencies may also require additional studies if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines.

These factors could cause us to incur higher costs and could cause the delay or termination of clinical studies, regulatory submissions, required approvals, or commercialization of our product candidates. Furthermore, if our suppliers fail to meet contractual requirements and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical studies may be delayed or we could lose potential revenue.

Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

Because we rely on third parties to develop and manufacture our product candidates, we must, at times, share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, collaborative research agreements, consulting agreements, letters of engagement, or other similar agreements with our collaborators, advisors, employees, and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, such as trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor’s discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business.

Risks Related to Commercialization of Our Product Candidates

If the market opportunities for our product candidates are smaller than we believe they are, our revenue may be adversely affected, and our business may suffer. Because the target patient populations of our product candidates are small, and the addressable patient population potentially even smaller, we must be able to successfully identify patients and acquire a significant market share to achieve profitability and growth.

We focus our research and product development on treatments for rare and ultra-rare genetic diseases. Given the small number of patients who have the diseases that we are targeting, it is critical to our ability to grow and become profitable that we continue to successfully identify patients with these rare and ultra-rare genetic diseases. Some of our current clinical programs may be most appropriate for patients with more severe forms of their disease. For instance, our Phase 2 study of UX007 in LC-FAOD enrolled patients with more severe disease. In addition, while adults make up the majority of the XLH patients, they often have less severe disease which may reduce the penetration of KRN23 in the adult population relative to the pediatric population. Given the overall rarity of the diseases we target, it is difficult to project the prevalence of the more severe forms, or the other subsets of patients that may be most suitable to address with our product candidates, which may further limit the addressable patient population to a small subset. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including the scientific literature, surveys of clinics, patient foundations, or market research, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these diseases. The number of patients may turn out to be lower than expected. The effort to identify patients with diseases we seek to treat is in early stages, and we cannot accurately predict the number of patients for whom treatment might be possible. Additionally, the potentially addressable patient population for each of our product candidates may be limited or may not be amenable to treatment with our product candidates, and new patients may become increasingly difficult to identify or gain access to, which would adversely affect our results of operations and our business. Further, even if we obtain significant market share for our product candidates, because the potential target populations are very small we may never become or remain profitable nor generate sufficient revenue growth to sustain our business.

We intend to rely on third-party manufacturers to produce our product candidates, but we have not entered into binding agreements with any such manufacturers to support commercialization. Additionally, these manufacturers do not have experience producing our product candidates at commercial levels and may not achieve the necessary regulatory approvals or produce our product candidates at the cost, quality, quantities, locations, and timing needed to support profitable commercialization.

We have not yet secured manufacturing capabilities for commercial quantities of our product candidates. Although we intend to rely on third-party manufacturers for commercialization, we have only entered into agreements with such manufacturers to support our clinical studies. We may be unable to negotiate binding agreements with the manufacturers to support our commercialization activities on commercially reasonable terms.

Manufacturers may not have the experience or ability to produce our product candidates at commercial levels. We may run into technical or scientific issues related to manufacturing or development that we may be unable to resolve in a timely manner or with available funds. We also have not completed all of the characterization and validation activities necessary for commercialization and regulatory approvals. If our manufacturing partners are not able to conduct all such necessary activities in accordance with applicable regulations, our commercialization efforts will be harmed.

Even if our third-party product manufacturers develop an acceptable manufacturing process, if such third-party manufacturers are unable to produce the necessary quantities of our product candidates, are unable to comply with GMP or other pertinent regulatory requirements, or are unable to produce our product candidates within our planned timeframe and cost parameters, the development and sales of our products, if approved, may be materially harmed.

Additionally, the cost to us for the supply of our product candidates manufactured by such third parties may be high and could limit our profitability, even if our third-party product manufacturers develop acceptable manufacturing processes that provide the necessary quantities of our product candidates in a compliant and timely manner. Furthermore, KHK is our sole supplier of commercial quantities of KRN23. The supply price to us for commercial sales of KRN23, which will be determined on a fixed double-digit percentage of net sales, will be higher than the typical cost of goods sold by companies focused on rare diseases.

We face intense competition and rapid technological change and the possibility that our competitors may develop therapies that are similar, more advanced, or more effective than ours, which may adversely affect our financial condition and our ability to successfully commercialize our product candidates.

The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. We are currently aware of various existing therapies that may compete with our product candidates. For example, XLH is currently treated with oral phosphate and Vitamin D therapy, which may compete with KRN23. Furthermore, B. Braun Medical Inc., or B. Braun, has received orphan drug designation for triheptanoin in Europe for certain LC-FAOD indications and we do not know if B. Braun is planning to initiate clinical development. Triheptanoin is also available in food-grade form, which may compete with our pharmaceutical-grade product. Investigator-sponsored trials evaluating triheptanoin in multiple indications are ongoing. LC-FAOD is currently treated with diet therapy and medium-chain triglyceride oil, which may compete with UX007. Glut1 DS is currently treated primarily with the ketogenic diet and anti-epileptic drugs, which may also compete with UX007. Additionally, we are aware of a

program at the National Institutes of Health that is investigating the use of another metabolite in the sialic acid pathway, ManNAc, for the treatment of GNE myopathy, which could compete with Ace-ER. The intellectual property rights for ManNAc are licensed to Escala Therapeutics, a subsidiary of Fortress Biotech, Inc., which acquired the rights from a company in New Zealand that manufactures ManNAc. Escala has received orphan designation for ManNAc in the United States and Europe for GNEM. ManNAc may have a potential advantage over Ace-ER in that it is not a charged molecule like sialic acid, which might improve ManNac's distribution and uptake. ManNac is also available for purchase from chemical supply and other companies, which may compete with Ace-ER. Gene therapy, gene correction, RNA-based therapies, and other approaches may also emerge for the treatment of any of the disease areas in which we focus.

We have competitors both in the United States and internationally, including major multinational pharmaceutical companies, specialty pharmaceutical companies, and biotechnology companies. Some of the pharmaceutical and biotechnology companies we expect to compete with include Shire, Sanofi, BioMarin, Alexion, and Roche, as well as other companies ranging from startups to large multinational companies. Many of our competitors have substantially greater financial, technical, and other resources, such as larger research and development staff and experienced marketing and manufacturing organizations. Additional mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. As a result, these companies may obtain regulatory approval more rapidly than we are able to and may be more effective in selling and marketing their products as well. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors may succeed in developing, acquiring, or licensing on an exclusive basis, products that are more effective or less costly than any product candidate that we may develop, or achieve earlier patent protection, regulatory approval, product commercialization, and market penetration than we do. Additionally, technologies developed by our competitors may render our potential product candidates uneconomical or obsolete, and we may not be successful in marketing our product candidates against competitors.

We are currently building an integrated commercial organization. If we are unable to establish sufficient field forces and marketing capabilities or enter into agreements with third parties to market and sell our product candidates, we may be unable to generate significant revenue.

Although our employees may have sold other similar products in the past while employed at other companies, we as a company have no experience selling and marketing our product candidates and we currently have minimal marketing and field force capacity. To successfully commercialize any products that may result from our development programs, we will need to develop these capabilities, either on our own or with others. If our product candidates receive regulatory approval, we intend to establish a marketing organization and field forces with technical expertise as well as supporting distribution capabilities to commercialize our product candidates in major markets, which will be expensive, difficult, and time consuming. Any failure or delay in the development of our internal field forces, marketing, and distribution capabilities would adversely impact the commercialization of our products.

Further, given our lack of prior experience in marketing and selling biopharmaceutical products, our initial estimate of the size of the required field force may be materially more or less than the size of the field force actually required to effectively commercialize our product candidates. As such, we may be required to hire large teams to adequately support the commercialization of our product candidates or we may incur excess costs as a result of hiring more commercial personnel than necessary. With respect to certain geographical markets, we may enter into collaborations with other entities to utilize their local marketing and distribution capabilities, but we may be unable to enter into such agreements on favorable terms, if at all. If our future collaborators do not commit sufficient resources to commercialize our future products, if any, and we are unable to develop the necessary marketing capabilities on our own, we will be unable to generate sufficient product revenue to sustain our business. We may be competing with companies that currently have extensive and well-funded marketing and sales operations. Without an internal team or the support of a third-party to perform key commercial functions, we may be unable to compete successfully against these more established companies.

The commercial success of any current or future product candidate will depend upon the degree of market acceptance by physicians, patients, third-party payors, and others in the medical community.

Even with the requisite approvals from the FDA and comparable foreign regulatory authorities, the commercial success of our product candidates will depend in part on the medical community, patients, and payors accepting our product candidates as medically useful, cost-effective, and safe. Any product that we bring to the market may not gain market acceptance by physicians, patients, payors, and others in the medical community. The degree of market acceptance of any of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy of the product as demonstrated in clinical studies and potential advantages over competing treatments;
- the prevalence and severity of any side effects, including any limitations or warnings contained in a product's approved labeling;
- the clinical indications for which approval is granted;
- relative convenience and ease of administration;
- the cost of treatment, particularly in relation to competing treatments;

- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the effectiveness of our field forces and marketing efforts;
- the strength of marketing and distribution support and timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments; and
- sufficient third-party insurance coverage and reimbursement.

Even if a potential product displays a favorable efficacy and safety profile in nonclinical and clinical studies, market acceptance of the product will not be fully known until after it is launched. Our efforts to educate the medical community and payors on the benefits of the product candidates may require significant resources and may never be successful. If our product candidates are approved but fail to achieve an adequate level of acceptance by physicians, patients, payors, and others in the medical community, we will not be able to generate sufficient revenue to become or remain profitable.

The insurance coverage and reimbursement status of newly approved products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for new or current products could limit our ability to market those products and decrease our ability to generate revenue.

Our target patient populations are small, and accordingly the pricing, coverage, and reimbursement of our product candidates, if approved, must be adequate to support our commercial infrastructure. Our per-patient prices must be sufficient to recover our development and manufacturing costs and potentially achieve profitability. Accordingly, the availability and adequacy of coverage and reimbursement by governmental and private payors are essential for most patients to be able to afford expensive treatments such as ours, assuming approval. Sales of our product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be paid for by health maintenance, managed care, pharmacy benefit, and similar healthcare management organizations, or reimbursed by government authorities, private health insurers, and other payors. If coverage and reimbursement are not available, or are available only to limited levels, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a return on our investment.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, the principal decisions about coverage and reimbursement for new drugs are typically made by the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, as CMS decides whether and to what extent a new drug will be covered and reimbursed under Medicare. Private payors tend to follow the coverage reimbursement policies established by CMS to a substantial degree. It is difficult to predict what CMS will decide with respect to reimbursement for products such as ours.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe, Canada, and other countries will put pressure on the pricing and usage of our product candidates. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medicinal products, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits.

Moreover, increasing efforts by governmental and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for new products approved and, as a result, they may not cover or provide adequate payment for our product candidates. We expect to experience pricing pressures in connection with the sale of any of our product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, and additional legislative changes. For example, within the last year, several states in the U.S. have introduced legislation to require pharmaceutical companies to disclose their costs to justify the prices of their products, and an "Affordable Drug Pricing Task-Force" has been formed in the U.S. House of Representatives with the goal of combating the increased costs of prescription drugs. The downward pressure on healthcare costs in general, and with respect to prescription drugs, surgical procedures, and other treatments in particular, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain effective patent rights for our product candidates or any future product candidates, we may not be able to compete effectively in our markets.

We rely upon a combination of patents, trade secret protection, and confidentiality agreements to protect the intellectual property related to our technologies and product candidates. Our success depends in large part on our and our licensors' ability to obtain and maintain patent and other intellectual property protection in the United States and in other countries with respect to our proprietary technology and products.

We have sought to protect our proprietary position by filing patent applications in the United States and abroad related to our novel technologies and products that are important to our business. This process is expensive and time consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain and involves complex legal and factual questions for which legal principles remain unsolved. The patent applications that we own or in-license may fail to result in issued patents with claims that cover our product candidates in the United States or in other foreign countries. There is no assurance that all potentially relevant prior art relating to our patents and patent applications has been found, which can invalidate a patent or prevent a patent from issuing from a pending patent application. Even if patents do successfully issue, and even if such patents cover our product candidates, third parties may challenge their validity, enforceability, or scope, which may result in such patents being narrowed, found unenforceable, or invalidated. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property, provide exclusivity for our product candidates, or prevent others from designing around our claims. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

We, independently or together with our licensors, have filed several patent applications covering various aspects of our product candidates. We cannot offer any assurances about which, if any, patents will issue, the breadth of any such patent or whether any issued patents will be found invalid and unenforceable or will be threatened by third parties. Any successful opposition to these patents or any other patents owned by or licensed to us after patent issuance could deprive us of rights necessary for the successful commercialization of any product candidates that we may develop. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate under patent protection could be reduced.

Although we have a number of patents or applications covering methods of use and certain compositions of matter, we do not have complete patent protection for our product candidates. For example, there are no issued patents and very limited pending applications for KRN23 in Latin America, where we have rights to commercialize the compound. Therefore, a competitor could develop the same or similar antibody as well as other approaches that target FGF23. Additionally, there are currently no issued patents that cover rhGUS or rhPPCA. Therefore, it is possible that a competitor could develop the same or similar enzyme with respect to rhGUS or rhPPCA, subject to any regulatory exclusivities. With respect to Ace-ER, none of the patents or applications relating to Ace-ER cover composition of matter. Therefore, it is possible that a competitor could develop the same or similar molecule. If we cannot obtain and maintain effective patent rights for our product candidates, we may not be able to compete effectively and our business and results of operations would be harmed.

We may not have sufficient patent terms to effectively protect our products and business.

Patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after it is filed. Although various extensions may be available, the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired for a product, we may be open to competition from generic medications.

While patent term extensions under the Hatch-Waxman Act in the United States and under supplementary protection certificates in Europe may be available to extend the patent exclusivity term for KRN23, rhGUS, UX007, and Ace-ER, we cannot provide any assurances that any such patent term extension will be obtained and, if so, for how long. In addition, upon issuance in the United States any patent term can be adjusted based on certain delays caused by the applicant(s) or the United States Patent and Trademark Office (USPTO). For example, a patent term can be reduced based on certain delays caused by the patent applicant during patent prosecution. If we do not have sufficient patent terms or regulatory exclusivity to protect our products, our business and results of operations will be adversely affected.

Patent policy and rule changes could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. The laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. We therefore cannot be certain that we or our licensors were the first to make the invention claimed in our owned and licensed patents or pending applications, or that we or our licensor were the first to file for patent protection of such inventions. Assuming the other requirements for patentability are met, in the United States prior to March 15, 2013, the first to make the claimed invention is entitled to the patent, while outside the United States, the first to file a patent application is entitled to the patent. After March 15, 2013, under the Leahy-Smith America Invents Act, or the Leahy-Smith Act, enacted on September 16, 2011, the United States has moved to a first to file system. The Leahy-Smith Act also includes a number of significant changes that affect the way patent applications will be prosecuted and may also affect patent litigation. The effects of these changes are currently unclear as the USPTO must still implement various regulations, the courts have yet to address any of these provisions and the applicability of the act and new regulations on specific patents discussed herein have not been determined and would need to be reviewed. In general, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

If we are unable to maintain effective proprietary rights for our product candidates or any future product candidates, we may not be able to compete effectively in our markets.

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable or that we elect not to patent, processes for which patents are difficult to enforce and any other elements of our product candidate discovery and development processes that involve proprietary know-how, information, or technology that is not covered by patents. However, trade secrets can be difficult to protect. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors, and contractors. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors.

Although we expect all of our employees and consultants to assign their inventions to us, and all of our employees, consultants, advisors, and any third parties who have access to our proprietary know-how, information, or technology to enter into confidentiality agreements, we cannot provide any assurances that all such agreements have been duly executed or that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Misappropriation or unauthorized disclosure of our trade secrets could impair our competitive position and may have a material adverse effect on our business. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret.

Claims of intellectual property infringement may prevent or delay our development and commercialization efforts.

Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of others. There have been many lawsuits and other proceedings involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions, and reexamination proceedings before the USPTO and corresponding foreign patent offices. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by other parties, exist in the fields in which we are developing product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of these other parties.

Other parties may assert that we are employing their proprietary technology without authorization. There may be patents or patent applications with claims to materials, formulations, methods of manufacture, or methods for treatment related to the use or manufacture of our product candidates. We have conducted freedom to operate analyses with respect to only certain of our product candidates, and therefore we do not know whether there are any patents of other parties that would impair our ability to commercialize all of our product candidates. We also cannot guarantee that any of our analyses are complete and thorough, nor can we be sure that we have identified each and every patent and pending application in the United States and abroad that is relevant or necessary to the commercialization of our product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our product candidates may infringe. For example, we are aware of a pending U.S. patent application by the Japan Health Sciences Foundation. Although we do not believe any valid and enforceable claim covering our product candidate will be issued from this U.S. application, we cannot guarantee that such claim will not issue.

In addition, other parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any of these patents were held by a court of competent jurisdiction to cover aspects of our formulations, the manufacturing process of any of our product candidates, methods of use, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtained a license under the applicable patents, or until such patents expire or are finally determined to be invalid or unenforceable. Such a license may not be available on commercially reasonable terms or at all.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products, or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure.

We may not be successful in obtaining or maintaining necessary rights to our product candidates through acquisitions and in-licenses.

We currently have rights to the intellectual property, through licenses from third parties and under patents that we own, to develop our product candidates. Because our programs may require the use of proprietary rights held by third parties, the growth of our business will likely depend in part on our ability to acquire, in-license, or use these proprietary rights. For example, our product candidates may require specific formulations to work effectively and efficiently and the rights to these formulations may be held by others. We may be unable to acquire or in-license any compositions, methods of use, processes, or other third-party intellectual property rights from third parties that we identify as necessary for our product candidates. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources, and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment.

We sometimes collaborate with U.S. and foreign academic institutions to accelerate our preclinical research or development under written agreements with these institutions. Typically, these institutions provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to pursue our program.

If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of that program and our business and financial condition could suffer.

We may face competition from biosimilars, which may have a material adverse impact on the future commercial prospects of KRN23, rhGUS, and rhPPCA.

Even if we are successful in achieving regulatory approval to commercialize a product candidate faster than our competitors, we may face competition from biosimilars with respect to KRN23, rhGUS, and rhPPCA. In the United States, the Biologics Price Competition and Innovation Act of 2009, or BPCI Act, created an abbreviated approval pathway for biological products that are demonstrated to be "highly similar," or biosimilar, to or "interchangeable" with an FDA-approved biological product. The BPCI Act prohibits the FDA from approving a biosimilar or interchangeable product that references a brand biological product until 12 years after the licensure of the reference product, but permits submission of an application for a biosimilar or interchangeable product to the FDA four years after the reference product was first licensed. The BPCI Act does not prevent another company from developing a product that is highly similar to the innovative product, generating its own data, and seeking approval. In the budget for fiscal year 2016, the Obama administration reasserted its proposal from prior years to cut this 12-year period of exclusivity down to seven years. The administration also reasserted a proposal to prohibit additional periods of exclusivity due to minor changes in product formulations, a practice often referred to as "evergreening." In October 2015, the United States agreed to the Trans-Pacific Partnership (TPP), an agreement with 11 other countries that addresses a variety of trade and economic issues. The TPP includes a provision that would require the signatory countries to provide a minimum of five years of exclusivity, and in some instances, eight years of exclusivity, to biological products. To come into effect, the TPP will require a requisite number of signatory countries to ratify the agreement; in the United States, such ratification, if it occurs, will be performed by Congress. It is possible that Congress could seek to harmonize the exclusivity periods in the TPP and the BPCI Act, or take other measures to modify or eliminate periods of exclusivity for biosimilar and interchangeable products. The BPCI Act is complex and is only beginning to be interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning is subject to uncertainty. Changes to the BPCI Act or the FDA's interpretation or implementation of the BPCI Act could have a material adverse effect on the future commercial prospects for KRN23, rhGUS, and rhPPCA.

In Europe, the European Commission has granted marketing authorizations for several biosimilars pursuant to a set of general and product class-specific guidelines for biosimilar approvals issued over the past few years. In Europe, a competitor may reference data supporting approval of an innovative biological product, but will not be able to get on the market until 10 years after the time of approval of the innovative product. This 10-year marketing exclusivity period will be extended to 11 years if, during the first eight of those 10 years, the marketing authorization holder obtains an approval for one or more new therapeutic indications that bring significant clinical benefits compared with existing therapies. In addition, companies may be developing biosimilars in other countries that could compete with our products.

If competitors are able to obtain marketing approval for biosimilars referencing our products, our products may become subject to competition from such biosimilars, with the attendant competitive pressure and consequences.

Additional competitors could enter the market with generic versions of our small-molecule product candidates, which may result in a material decline in sales of UX007 and Ace-ER.

Under the Hatch-Waxman Act, a pharmaceutical manufacturer may file an abbreviated new drug application, or ANDA, seeking approval of a generic copy of an approved innovator product. Under the Hatch-Waxman Act, a manufacturer may also submit an NDA under section 505(b)(2) that references the FDA's finding of safety and effectiveness of a previously approved drug. A 505(b)(2) NDA product may be for a new or improved version of the original innovator product. Innovative small molecule drugs may be eligible for certain periods of regulatory exclusivity (e.g., five years for new chemical entities, three years for changes to an approved drug requiring a new clinical study, seven years for orphan drugs), which preclude FDA approval (or in some circumstances, FDA filing and review of) an ANDA or 505(b)(2) NDA relying on the FDA's finding of safety and effectiveness for the innovative drug. In addition to the benefits of regulatory exclusivity, an innovator NDA holder may have patents claiming the active ingredient, product formulation or an approved use of the drug, which would be listed with the product in the "Orange Book." If there are patents listed in the Orange Book, a generic applicant that seeks to market its product before expiration of the patents must include in the ANDA or 505(b)(2) what is known as a "Paragraph IV certification," challenging the validity or enforceability of, or claiming non-infringement of, the listed patent or patents. Notice of the certification must be given to the innovator, too, and if within 45 days of receiving notice the innovator sues to protect its patents, approval of the ANDA is stayed for 30 months, or as lengthened or shortened by the court.

Accordingly, if UX007 and Ace-ER are approved, competitors could file ANDAs for generic versions of UX007 and Ace-ER, or 505(b)(2) NDAs that reference UX007 and Ace-ER, respectively. If there are patents listed for UX007 and Ace-ER in the Orange Book, those ANDAs and 505(b)(2) NDAs would be required to include a certification as to each listed patent indicating whether the ANDA applicant does or does not intend to challenge the patent. We cannot predict whether any patents issuing from our pending patent applications will be eligible for listing in the Orange Book, how any generic competitor would address such patents, whether we would sue on any such patents, or the outcome of any such suit.

We may not be successful in securing or maintaining proprietary patent protection for products and technologies we develop or license. Moreover, if any patents that are granted and listed in the Orange Book are successfully challenged by way of a Paragraph IV certification and subsequent litigation, the affected product could more immediately face generic competition and its sales would likely decline materially. Should sales decline, we may have to write off a portion or all of the intangible assets associated with the affected product and our results of operations and cash flows could be materially and adversely affected.

The patent protection and patent prosecution for some of our product candidates is dependent on third parties.

While we normally seek and gain the right to fully prosecute the patents relating to our product candidates, there may be times when patents relating to our product candidates are controlled by our licensors. This is the case with our agreement with KHK, who is primarily responsible for the prosecution of patents and patent applications licensed to us under the collaboration agreement. If KHK or any of our future licensing partners fail to appropriately prosecute and maintain patent protection for patents covering any of our product candidates, our ability to develop and commercialize those product candidates may be adversely affected and we may not be able to prevent competitors from making, using, and selling competing products. In addition, even where we now have the right to control patent prosecution of patents and patent applications we have licensed from third parties, we may still be adversely affected or prejudiced by actions or inactions of our licensors and their counsel that took place prior to us assuming control over patent prosecution.

If we fail to comply with our obligations in the agreements under which we license intellectual property and other rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.

We are a party to a number of intellectual property license agreements that are important to our business and expect to enter into additional license agreements in the future. Our existing license agreements impose, and we expect that future license agreements will impose, various diligence, milestone payment, royalty, and other obligations on us. If we fail to comply with our obligations under these agreements, or we are subject to a bankruptcy, we may be required to make certain payments to the licensor, we may lose the exclusivity of our license, or the licensor may have the right to terminate the license, in which event we would not be able to develop or market products covered by the license. Additionally, the milestone and other payments associated with these licenses will make it less profitable for us to develop our drug candidates. See "Business—License Agreements" in our most recent Annual Report on Form 10-K for a description of our license agreements with KHK, Baylor Research Institute, Nobelpharma, Alcami, HIBM Research Group, St. Louis University, and St. Jude Children's Research Hospital, which includes a description of the termination provisions of these agreements.

In some cases, patent prosecution of our licensed technology is controlled solely by the licensor. If our licensors fail to obtain and maintain patent or other protection for the proprietary intellectual property we license from them, we could lose our rights to the intellectual property or our exclusivity with respect to those rights, and our competitors could market competing products using the intellectual property. In certain cases, we control the prosecution of patents resulting from licensed technology. In the event we breach any of our obligations related to such prosecution, we may incur significant liability to our licensing partners. Licensing of intellectual property is of critical importance to our business and involves complex legal, business, and scientific issues. Disputes may arise regarding intellectual property subject to a licensing agreement, including but not limited to:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our collaborators; and
- the priority of invention of patented technology.

If disputes over intellectual property and other rights that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates.

Although we are not currently involved in any litigation, we may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time consuming, and unsuccessful.

Competitors may infringe our patents or the patents of our licensors. Although we are not currently involved in any litigation, if we or one of our licensing partners were to initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. The outcome following legal assertions of invalidity and unenforceability is unpredictable.

Interference proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise sufficient capital to continue our clinical studies, continue our research programs, license necessary technology from third parties, or enter into development partnerships that would help us bring our product candidates to market.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions, or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock.

We may be subject to claims that our employees, consultants, or independent contractors have wrongfully used or disclosed confidential information of third parties or that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

We employ certain individuals who were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants, and independent contractors do not use the proprietary information or know-how of others in their work for us, and we are not currently subject to any claims that our employees, consultants, or independent contractors have wrongfully used or disclosed confidential information of third parties, we may in the future be subject to such claims. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could adversely impact our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

We may be subject to claims challenging the inventorship of our patents and other intellectual property.

Although we are not currently experiencing any claims challenging the inventorship of our patents or ownership of our intellectual property, we may in the future be subject to claims that former employees, collaborators or other third parties have an interest in our patents or other intellectual property as an inventor or co-inventor. For example, we may have inventorship disputes arise from conflicting obligations of consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology industry involves both technological and legal complexity. Therefore, obtaining and enforcing biotechnology patents is costly, time consuming, and inherently uncertain. In addition, the United States has recently enacted and is currently implementing wide-ranging patent reform legislation. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty about our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on future actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting, and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Further, licensing partners such as KHK may not prosecute patents in certain jurisdictions in which we may obtain commercial rights, thereby precluding the possibility of later obtaining patent protection in these countries. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and may also export infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Risks Related to Our Business Operations

Our future success depends in part on our ability to retain our Founder, President, and Chief Executive Officer and to attract, retain, and motivate other qualified personnel.

We are dependent on Emil D. Kakkis, M.D., Ph.D., our Founder, President, and Chief Executive Officer, the loss of whose services may adversely impact the achievement of our objectives. Dr. Kakkis could leave our employment at any time, as he is an "at will" employee. Recruiting and retaining other qualified employees, consultants, and advisors for our business, including scientific and technical personnel, will also be critical to our success. There is currently a shortage of skilled personnel in our industry, which is likely to continue. As a result, competition for skilled personnel is intense and the turnover rate can be high. We may not be able to attract and retain personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for individuals with similar skill sets. In addition, failure to succeed in preclinical or clinical studies may make it more challenging to recruit and retain qualified personnel. The inability to recruit and retain qualified personnel, or the loss of the services of Dr. Kakkis, may impede the progress of our research, development, and commercialization objectives.

If we fail to obtain or maintain orphan drug exclusivity for our products, our competitors may sell products to treat the same conditions and our revenue will be reduced.

Our business strategy focuses on the development of drugs that are eligible for FDA and EU orphan drug designation. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is intended to treat a rare disease or condition, defined as a patient population of fewer than 200,000 in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the EU, the EMA's Committee for Orphan Medicinal Products for Human Use grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention, or treatment of a life-threatening or chronically debilitating condition when the prevalence of the condition is not more than five in 10,000 persons in the EU or when, without incentives, it is unlikely that sales of the drug in the EU would be sufficient to justify the necessary investment in developing the drug or biological product. Additionally, there must be no satisfactory method of diagnosis, prevention, or treatment, or, if such a method exists, the medicine must be of significant benefit to those affected by the condition. In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical study costs, tax advantages, and user-fee waivers. In addition, if a product receives the first FDA approval for the indication for which it has orphan designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity or where the manufacturer is unable to assure sufficient product quantity. In the EU, orphan drug designation entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity following drug or biological product approval. This period may be reduced to six years if the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity.

Because the extent and scope of patent protection for our products may in some cases be limited, orphan drug designation is especially important for our products for which orphan drug designation may be available. For eligible drugs, we plan to rely on the exclusivity period under the Orphan Drug Act to maintain a competitive position. If we do not obtain orphan drug exclusivity for our drug products and biologic products that do not have broad patent protection, our competitors may then sell the same drug to treat the same condition sooner than if we had obtained orphan drug exclusivity and our revenue will be reduced.

Even though we have orphan drug designation for UX007 for the treatment of fatty acid oxidation disorders in the United States, as well as for UX007 for the treatment of Glut1 DS, KRN23, rhGUS, and Ace-ER in the United States and Europe, we may not be the first to obtain marketing approval for any particular orphan indication due to the uncertainties associated with developing pharmaceutical products. Further, even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties can be approved for the same condition or the same drug can be approved for a different indication unless there are other exclusivities such as new chemical entity exclusivity preventing such approval. Even after an orphan drug is approved, the FDA or EMA can subsequently approve the same drug with the same active moiety for the same condition if the FDA or EMA concludes that the later drug is safer, more effective, or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

We will need to expand our organization and we may experience difficulties in managing this growth, which could disrupt our operations.

As of June 30, 2016, we had 329 full-time employees. As our development and commercialization plans and strategies develop, we expect to need additional managerial, operational, field forces, marketing, financial, legal, and other resources. Our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, operational mistakes, loss of business opportunities, loss of employees, and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and/or grow revenue could be reduced, and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize product candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth.

We may not be successful in our efforts to identify, license, discover, develop, or commercialize additional product candidates.

Although a substantial amount of our effort will focus on the continued clinical testing, potential approval, and commercialization of our existing product candidates, the success of our business also depends upon our ability to identify, license, discover, develop, or commercialize additional product candidates. Research programs to identify and develop new product candidates, such as those under our collaboration with Arcturus, requires substantial technical, financial, and human resources. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful. Our research programs or licensing efforts may fail to yield additional product candidates for clinical development and commercialization for a number of reasons, including but not limited to the following:

- our research or business development methodology or search criteria and process may be unsuccessful in identifying potential product candidates;
- we may not be able or willing to assemble sufficient technical, financial or human resources to acquire or discover additional product candidates;
- we may face competition in obtaining and/or developing additional product candidates;
- our product candidates may not succeed in research, discovery, preclinical or clinical testing;
- our potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval;
- competitors may develop alternatives that render our product candidates obsolete or less attractive;
- product candidates we develop may be covered by third parties' patents or other exclusive rights;
- the market for a product candidate may change during our program so that such a product may become unreasonable to continue to develop;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost or at all; and
- a product candidate may not be accepted as safe and effective by regulatory authorities, patients, the medical community, or payors.

If any of these events occur, we may be forced to abandon our development efforts for a program or programs, or we may not be able to identify, license, discover, develop, or commercialize additional product candidates, which would have a material adverse effect on our business and could potentially cause us to cease operations.

We incur increased costs as a result of operating as a public company, and our management is now required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company, we incur significant legal, accounting, and other expenses. We are required to comply with several supplemental requirements that will necessitate additional resources and management time and expense. These supplemental requirements include providing full executive compensation disclosure, such as Compensation, Discussion & Analysis section in our proxy statement for the annual meeting of stockholders; a say-on-frequency vote; a say-on-pay vote beginning with this year's Annual Meeting of Stockholders; and pay-ratio disclosure beginning with our 2018 Annual Meeting of Stockholders. We will also be subject to rules subsequently implemented by the SEC and The NASDAQ Global Select Market. In addition, the current political environment, and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate. Our management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased our legal and financial compliance costs and will make some activities more time consuming and costly. For example, being a public company could make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain adequate levels of such coverage.

Additionally, the Sarbanes-Oxley Act requires, among other things, that we maintain effective internal controls for financial reporting and disclosure controls and procedures. In particular, we are required to perform system and process evaluation and testing of our internal controls over financial reporting to allow management to report on the effectiveness of our internal controls over financial reporting, as required by Section 404(a) of the Sarbanes-Oxley Act. We are now also subject to the compliance requirements of Section 404(b) of the Sarbanes-Oxley Act, which has resulted in us incurring substantial expenses and expending significant management efforts to comply with the Act, which we will continue. We currently do not have an internal audit group, and we will need to hire additional accounting and financial staff with appropriate public company experience and technical accounting knowledge. If we are not able to comply with the requirements of Section 404(b) or if we identify or our independent registered public accounting firm identifies deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses, the market price of our stock could decline and we could be subject to sanctions or investigations by NASDAQ, the SEC, or other regulatory authorities, which would require additional financial and management resources.

Changes to healthcare and FDA laws, regulations, and policies may have a material adverse effect on our business and results of operations.

United States

In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs and to modify the regulation of drug and biologic products. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or the PPACA, was passed, which substantially changes the way health care is financed by both governmental and private insurers, and significantly impacts the U.S. pharmaceutical industry. The PPACA, among other things, subjects biologic products to potential competition by lower-cost biosimilars, addresses a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted, or injected, increases the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extends the rebate program to individuals enrolled in Medicaid managed care organizations, establishes annual fees and taxes on manufacturers of certain branded prescription drugs, and promotes a new Medicare Part D coverage gap discount program.

The Consolidated Appropriations Act, signed into law on December 18, 2015, modifies certain provisions of the PPACA; the new appropriations law suspends or delays several taxes, including the excise tax on high cost employer-sponsored health coverage, which were expected to generate significant funds for the PPACA. Implementation of the PPACA remains ongoing, and there remains uncertainty as to how the law's various provisions will ultimately affect the industry.

In addition, other legislative changes have been adopted in the United States to contain healthcare costs. On August 2, 2011, the Budget Control Act of 2011, among other things, required reductions in federal spending, which eventually triggered Medicare sequestration—the requirement to reduce Medicare payments to providers up to 2% per fiscal year. Following an executive order by President Obama on March 1, 2013, the 2% Medicare payment reductions were applied to fee-for-service claims with dates of service or dates of discharge on or after April 1, 2013. Sequestration was initially set to expire in fiscal year 2021 but was extended, most recently by the Bipartisan Budget Act of 2015, which extends Medicare sequestration to 2025. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, and which could result in reduced demand for our product candidates or additional pricing pressures.

In addition, the FDA's laws, regulations, and policies remain the subject of agency and legislative proposals for reform, which could affect our product development, testing, marketing approvals, and post-market activities. For example, as discussed in the risk factor entitled "***We may face competition from biosimilars, which may have a material adverse impact on the future commercial prospects of KRN23, rhGUS, and rhPPCA***", there are proposals to reduce the exclusivity protections provided to biosimilar and interchangeable biologic products, and FDA has begun to issue policies regarding key aspects of the regulation of these products. Congress also is considering various proposals relating to FDA's premarket approval process and other issues. For example, the 21st Century Cures Act, which passed the U.S. House of Representatives in July 2015, proposes a wide range of reforms, such as broadening the types of data required to support drug approval, extending protections from genetic competition, accelerating approval of breakthrough therapies, expanding the orphan drug product program, and clarifying how manufacturers communicate about their products. It is uncertain whether these or similar proposals will be passed into law.

European Union

In the EU, the European Commission adopted the Commission Delegated Regulation (EU) No 2016/161 of 2 October 2015, supplementing Directive 2001/83/EC of the European Parliament and of the Council by laying down detailed rules for the safety features appearing on the packaging of medicinal products for human use. The Regulation lays down the rules for the features appearing on the packaging of these medicinal products, including, inter alia, the characteristics and technical specifications of the unique identifier that enables the authenticity of medicinal products to be verified and individual packs to be identified, the modalities for the verification of the safety features, and the list of medicinal products and product categories subject and not subject to prescription which shall not bear and bear (respectively) safety features.

The European Commission has also launched a series of public consultations that are aimed to the adoption of Notices and Guidelines which will serve the interpretation of currently applicable Regulations and Directives.

For example, from August 28, 2015 with closing date November 24, 2015 the European Commission launched four public consultations which concerned good manufacturing practices and clinical trials for human medicinal products. From November 16, 2015 to February 15, 2016, the European Commission opened a public consultation from the Commission on certain aspects of the application of Articles 3, 5 and 7 of Regulation (EC) No 141/2000 on orphan medicinal products. The purpose of the Consultation is to review the 2003 Communication on orphan medicinal products (which will be replaced with a Notice), in order to streamline the regulatory framework and to adapt the Communication to technical progress. The consultation focuses on a variety of elements of Regulation (EC) No 141/2000, which include the encouragement of development of orphan medicinal products for communicable diseases and the simplification of the procedure for the reassessment of orphan criteria when two authorization application procedures are pending in parallel for two orphan medicinal products.

We may be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, and health information privacy and security laws. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

If we obtain FDA approval for any of our product candidates and begin commercializing those products in the United States, our operations may be directly, or indirectly through our customers, subject to various federal and state fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute, the federal False Claims Act, and physician sunshine laws and regulations. These laws may impact, among other things, our proposed field, marketing, and education programs. In addition, we may be subject to patient privacy regulation by both the federal government and the states in which we conduct our business. The laws that may affect our ability to operate include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering, or paying remuneration, directly or indirectly, to induce, or in return for, the purchase or recommendation of an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;
- federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other payors that are false or fraudulent;
- the Health Insurance Portability and Accountability Act (HIPAA), which created new federal criminal statutes that prohibit executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and its implementing regulations, which imposes certain requirements relating to the privacy, security, and transmission of individually identifiable health information;
- the federal physician sunshine requirements under the PPACA requires manufacturers of drugs, devices, biologics, and medical supplies to report annually to the U.S. Department of Health and Human Services information related to payments and other transfers of value to physicians, other healthcare providers, and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members and applicable group purchasing organizations; and
- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws that may apply to items or services reimbursed by any payor, including commercial insurers, state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. In addition, recent health care reform legislation has strengthened these laws. For example, the PPACA, among other things, amends the intent requirement of the federal anti-kickback and criminal healthcare fraud statutes. A person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it. Moreover, the PPACA provides that the government may assert that a claim including items or services resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim for purposes of the False Claims Act.

If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from participation in government health care programs, such as Medicare and Medicaid, imprisonment, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

International expansion of our business exposes us to business, regulatory, political, operational, financial, and economic risks associated with doing business outside of the United States.

We currently have limited international operations, but our business strategy incorporates potentially significant international expansion, particularly in anticipation of approval of our product candidates. We currently conduct physician and patient association outreach activities, as well as clinical studies, outside of the United States and plan to maintain field forces representatives internationally in the future. Doing business internationally involves a number of risks, including but not limited to:

- multiple, conflicting, and changing laws and regulations such as privacy regulations, tax laws, export and import restrictions, employment laws, regulatory requirements, and other governmental approvals, permits, and licenses;
- introductions of new Health Authority requirements and/or changes in Health Authority expectations;
- failure by us to obtain and maintain regulatory approvals for the use of our products in various countries;
- additional potentially relevant third-party patent rights;
- complexities and difficulties in obtaining protection and enforcing our intellectual property;
- difficulties in staffing and managing foreign operations;
- complexities associated with managing multiple payor reimbursement regimes, government payors, or patient self-pay systems;
- limits in our ability to penetrate international markets;
- financial risks, such as longer payment cycles, difficulty collecting accounts receivable, the impact of local and regional financial crises on demand and payment for our products, and exposure to foreign currency exchange rate fluctuations;
- natural disasters and political and economic instability, including wars, terrorism, political unrest, outbreak of disease, boycotts, curtailment of trade, and other business restrictions;
- certain expenses including, among others, expenses for travel, translation, and insurance;
- regulatory and compliance risks that relate to maintaining accurate information and control over commercial operations and activities that may fall within the purview of the U.S. Foreign Corrupt Practices Act, or FCPA, its books and records provisions, or its anti-bribery provisions; and
- regulatory and compliance risks relating to doing business with any entity that is subject to sanctions administered by the Office of Foreign Assets Control of the U.S. Department of the Treasury.

Any of these factors could significantly harm our future international expansion and operations and, consequently, our results of operations.

We may incur additional tax liabilities related to our operations.

We are subject to income tax in the United States and various foreign jurisdictions. Significant judgment is required in determining our worldwide tax liabilities, and our effective tax rate is derived from a combination of the applicable statutory rates in the various jurisdictions in which we operate. We record liabilities that involve significant management judgment for uncertain tax positions. The IRS or other domestic or foreign taxing authorities may disagree with our interpretation of tax law as applied to our operations or with the positions we may take with respect to particular tax issues on our tax returns. Consequently, our reported effective tax rate and our after-tax cash flows may be materially and adversely affected by tax assessments or judgments in excess of accrued amounts we have estimated in preparing our financial statements. Further, our effective tax rate may also be adversely affected.

Our effective tax rate is derived from a combination of the applicable statutory rates in the various jurisdictions in which we operate. Such rate may be adversely affected by numerous factors, including changes in our operating structure, changes in the mix of our earnings among countries with differing statutory rates, including those resulting from our intercompany transfer pricing or from changes in the rules governing transfer pricing, the repatriation of non-U.S. earnings for which we have not previously provided for U.S. taxes, the availability of the U.S. research and development tax credit, and other changes in tax laws and regulations. We cannot give any assurance as to what our effective tax rate will be in the future because, among other things, there is uncertainty regarding the tax policies of the jurisdictions where we operate. Changes in tax laws, such as tax reform in the United States or changes in tax laws resulting from the Organization for Economic Co-operation and Development’s multi-jurisdictional plan of action to address base erosion and profit shifting, could impact our effective tax rate. Any significant increase in our future effective tax rate could reduce net income for future periods and may have a material adverse impact on our results of our operations.

If we fail to comply with environmental, health, and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

Our research and development activities and our third-party manufacturers' and suppliers' activities involve the controlled storage, use, and disposal of hazardous materials, including the components of our product candidates and other hazardous compounds. We and our manufacturers and suppliers are subject to laws and regulations governing the use, manufacture, storage, handling, and disposal of these hazardous materials. In some cases, these hazardous materials and various wastes resulting from their use are stored at our or our manufacturers' facilities pending their use and disposal. We cannot eliminate the risk of contamination, which could cause an interruption of our commercialization efforts, research and development efforts, and business operations or environmental damage that could result in costly clean-up and liabilities under applicable laws and regulations governing the use, storage, handling, and disposal of these materials and specified waste products. Although we believe that the safety procedures utilized by us and our third-party manufacturers for handling and disposing of these materials generally comply with the standards prescribed by these laws and regulations, we cannot guarantee that this is the case or eliminate the risk of accidental contamination or injury from these materials. In such an event, we may be held liable for any resulting damages—and such liability could exceed our resources—and state or federal or other applicable authorities may curtail our use of certain materials and/or interrupt our business operations. Furthermore, environmental laws and regulations are complex, change frequently, and have tended to become more stringent. We cannot predict the impact of such changes and cannot be certain of our future compliance. We do not currently carry biological or hazardous waste insurance coverage.

Risks generally associated with a company-wide implementation of an enterprise resource planning (ERP) system may adversely affect our business and results of operations or the effectiveness of our internal controls over financial reporting.

We are in the process of implementing a company-wide ERP system to upgrade certain existing business, operational, and financial processes. Our ERP implementation is a complex and time-consuming project that we expect will require more than a year to complete. Our results of operations could be adversely affected if we experience time delays or cost overruns during the ERP implementation process, or if the ERP system or associated process changes do not give rise to the benefits that we expect. This project has required and may continue to require investment of capital and human resources, the re-engineering of processes of our business, including our procurement process, and the attention of many employees who would otherwise be focused on other aspects of our business. Any deficiencies in the design and implementation of the new ERP system could result in potentially much higher costs than we had incurred and could adversely affect our ability to develop and launch solutions, provide services, fulfill contractual obligations, file reports with the SEC in a timely manner, operate our business or otherwise affect our controls environment. Any of these consequences could have an adverse effect on our results of operations and financial condition.

Our business and operations may be materially adversely affected in the event of computer system failures or security breaches.

Despite the implementation of security measures, our internal computer systems, and those of our contract research organizations and other third parties on which we rely, are vulnerable to damage from computer viruses, unauthorized access, cyber-attacks, natural disasters, fire, terrorism, war, and telecommunication and electrical failures. If such an event were to occur and interrupt our operations, it could result in a material disruption of our drug development programs. For example, the loss of clinical trial data from ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, including protected health information or personal data of employees or former employees, we could incur liability and the further development of our drug candidates could be delayed. We may also be vulnerable to cyber- attacks by hackers or other malfeasance. This type of breach of our cybersecurity may compromise our confidential information and/or our financial information and adversely affect our business or result in legal proceedings.

We or the third parties upon whom we depend may be adversely affected by earthquakes or other natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Our corporate headquarters and laboratory are located in the San Francisco Bay Area, and our collaboration partner for KRN23, KHK, is located in Japan, which have both in the past experienced severe earthquakes and other natural disasters. We do not carry earthquake insurance. Earthquakes or other natural disasters could severely disrupt our operations or those of our collaborators, and have a material adverse effect on our business, results of operations, financial condition, and prospects. If a natural disaster, power outage, or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure (such as the manufacturing facilities of our third-party contract manufacturers) or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place currently are limited and are unlikely to prove adequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business.

Risks Related to Ownership of Our Common Stock

The market price of our common stock may be highly volatile.

The market price of our common stock has been, and is likely to continue to be, volatile, including for reasons unrelated to changes in our business. Our stock price could be subject to wide fluctuations in response to a variety of factors, including but not limited to the following:

- adverse results or delays in preclinical or clinical studies;
- any inability to obtain additional funding;
- any delay in filing an IND, NDA, BLA, MAA, or other regulatory submission for any of our product candidates and any adverse development or perceived adverse development with respect to the applicable regulatory agency's review of that IND, NDA, BLA, MAA, or other regulatory submission;
- the perception of limited market sizes or pricing for our product candidates;
- failure to successfully develop and commercialize our product candidates;
- the level of any revenue we receive from named patient sales;
- post-marketing safety issues;
- failure to maintain our existing strategic collaborations or enter into new collaborations;
- failure by us or our licensors and strategic collaboration partners to prosecute, maintain, or enforce our intellectual property rights;
- changes in laws or regulations applicable to our products;
- any inability to obtain adequate product supply for our product candidates or the inability to do so at acceptable prices;
- adverse regulatory decisions;
- introduction of new products, services, or technologies by our competitors;
- failure to meet or exceed financial projections we may provide to the public;
- failure to meet or exceed the financial projections of the investment community;
- the perception of the pharmaceutical industry by the public, legislatures, regulators, and the investment community;
- announcements of significant acquisitions, strategic partnerships, joint ventures, or capital commitments by us, our strategic collaboration partner, or our competitors;
- disputes or other developments relating to proprietary rights, including patents, litigation matters, and our ability to obtain patent protection for our technologies;
- additions or departures of key scientific or management personnel;
- significant lawsuits, including patent or stockholder litigation;
- securities or industry analysts' reports regarding our stock, or their failure to issue such reports;
- changes in the market valuations of similar companies;
- general market or macroeconomic conditions;
- sales of our common stock by us or our stockholders in the future; and
- trading volume of our common stock.

In addition, biotechnology and biopharmaceutical companies in particular have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance.

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.

We will need additional capital in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell common stock, convertible securities, or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities, or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. These sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders.

Pursuant to our 2014 Incentive Plan, or the 2014 Plan, our management is authorized to grant stock options and other equity-based awards to our employees, directors, and consultants. An aggregate of 2,250,000 shares were available for issuance at the inception of the 2014 Plan. The number of shares available for future grant under the 2014 Plan will automatically increase on January 1 of each year (as of January 1, 2015) by the lesser of 2,500,000 shares or 4% of all shares of our capital stock outstanding as of December 31 of the prior calendar year, subject to the ability of our compensation committee to take action to reduce the size of the increase in any given year. Currently, we plan to register the increased number of shares available for issuance under the 2014 Plan each year.

Pursuant to our 2014 Employee Stock Purchase Plan, or 2014 ESPP, eligible employees can acquire shares of our common stock at a discount to the prevailing market price, and an aggregate of 600,000 shares were available for issuance at the inception of the 2014 ESPP. The number of shares available for issuance under the 2014 ESPP will automatically increase on January 1 of each year (as of January 1, 2015) by the lesser of 1,200,000 shares or 1% of all shares of our capital stock outstanding as of December 31 of the prior calendar year, subject to the ability of our compensation committee to take action to reduce the size of the increase in any given year. If our board of directors elects to increase the number of shares available for future grant under the 2014 Plan or the 2014 ESPP, our stockholders may experience additional dilution, which could cause our stock price to fall.

Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.

We have incurred substantial losses during our history and do not expect to become profitable in the near future nor may we ever achieve profitability. To the extent that we continue to generate taxable losses, unused taxable losses will, subject to certain limitations, carry forward to offset future taxable income, if any, until such unused losses expire. Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an "ownership change," generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards, or NOL carryforwards, and other pre-change tax attributes (such as research tax credits) to offset its post-change income may be limited. An analysis to determine limitations upon our NOL carryforwards and other pre-change tax attributes for ownership changes that have occurred previously has been performed, resulting in a permanent decrease of federal and state NOL carryforwards in the amount of $6.9 million and a permanent decrease in federal research tax credit carryforwards in the amount of $0.3 million. As a result of these decreases and others that may occur as a result of future ownership changes, our ability to use our pre-change NOL carryforwards and other tax attribute carryforwards to offset U.S. federal taxable income and tax liabilities is limited and may become subject to even greater limitations, which could potentially accelerate or permanently increase future federal tax liabilities for us. In addition, there may be periods during which the use of state income tax NOL carryforwards and other state tax attribute carryforwards (such as state research tax credits) are suspended or otherwise limited, which could potentially accelerate or permanently increase future state tax liabilities for us.

We do not intend to pay dividends on our common stock so any returns will be limited to the value of our stock.

We have never declared or paid any cash dividends on our common stock. We currently intend to retain all available funds and any future earnings, if any, for the development, operation, and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to stockholders will therefore be limited to the appreciation of their stock.

Provisions in our amended and restated certificate of incorporation and by-laws, as well as provisions of Delaware law, could make it more difficult for a third-party to acquire us or increase the cost of acquiring us, even if doing so would benefit our stockholders or remove our current management.

Our amended and restated certificate of incorporation, amended and restated by-laws, and Delaware law contain provisions that may have the effect of delaying or preventing a change in control of us or changes in our management. Our amended and restated certificate of incorporation and by-laws include provisions that:

- authorize "blank check" preferred stock, which could be issued by our board of directors without stockholder approval and may contain voting, liquidation, dividend, and other rights superior to our common stock;
- create a classified board of directors whose members serve staggered three-year terms;
- specify that special meetings of our stockholders can be called only by our board of directors or the chairperson of our board of directors;
- prohibit stockholder action by written consent;
- establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors;
- provide that our directors may be removed only for cause;
- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum;
- specify that no stockholder is permitted to cumulate votes at any election of directors;

- expressly authorize our board of directors to modify, alter or repeal our amended and restated by-laws; and
- require holders of 75% of our outstanding common stock to amend specified provisions of our amended and restated certificate of incorporation and amended and restated by-laws.

These provisions, alone or together, could delay, deter, or prevent hostile takeovers and changes in control or changes in our management.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15% of our outstanding voting stock to merge or combine with us.

Any provision of our amended and restated certificate of incorporation or amended and restated by-laws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock.

Item 2. UNREGISTERED SALES OF EQUITY SECURITIES AND USE OF PROCEEDS

Unregistered Sales of Equity Securities

None.

ITEM 3. DEFAULTS UPON SENIOR SECURITIES

None.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

ITEM 5. OTHER INFORMATION

None.

Item 6. EXHIBITS

Exhibit Number	Exhibit Description	Incorporated by Reference			Furnished or Filed Herewith
		Form	Date	Number	
3.1	Amended and Restated Certificate of Incorporation of Ultragenyx Pharmaceutical Inc.	8-K	2/5/2014	3.1	
3.2	Ultragenyx Pharmaceutical Inc. Amended and Restated Bylaws	8-K	2/5/2014	3.2	
10.1†	License and Collaboration Agreement by and between Takeda Pharmaceutical Company Limited and Ultragenyx Pharmaceutical Inc., dated June 6, 2016				X
10.2†	Common Stock Purchase Agreement between Ultragenyx Pharmaceutical Inc. and Takeda Pharmaceutical Company Limited, dated as of June 6, 2016				X
10.3#	Offer letter, dated as of April 26, 2016, between the Registrant and Karah Parschauer				X
10.4	Sales Agreement, dated as of July 1, 2016, between Ultragenyx Pharmaceutical Inc. and Cowen and Company, LLC	8-K	7/5/2016	1.1	
31.1	Certification of Principal Executive Officer Required Under Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as amended				X
31.2	Certification of Principal Financial Officer Required Under Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as amended				X
32.1*	Certification of Principal Executive Officer and Principal Financial Officer Required Under Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, and 18 U.S.C. 1350				X
101.INS	XBRL Instance Document				X
101.SCH	XBRL Taxonomy Extension Schema Document				X
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document				X
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document				X
101.LAB	XBRL Taxonomy Extension Labels Linkbase Document				X
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document				X

* The certification attached as Exhibit 32.1 that accompanies this Quarterly Report on Form 10-Q is furnished to, and not deemed filed with the SEC and is not to be incorporated by reference into any filing of Registrant under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Form 10-Q, irrespective of any general incorporation language contained in such filing.

† Portions of this exhibit (indicated by asterisks) have been omitted pursuant to a request for confidential treatment, and this exhibit has been filed separately with the SEC.

# Indicates management contract or compensatory plan

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

ULTRAGENYX PHARMACEUTICAL INC.

Date: August 8, 2016

By: /s/ Emil D. Kakkis
Emil D. Kakkis, M.D., Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Date: August 8, 2016

By: /s/ Shalini Sharp
Shalini Sharp
Executive Vice President and Chief Financial Officer
(Principal Financial Officer)

Date: August 8, 2016

By: /s/ Theodore A. Huizenga
Theodore A. Huizenga
Executive Director, Corporate Controller
(Principal Accounting Officer)

LICENSE AND COLLABORATION AGREEMENT

BY AND BETWEEN

TAKEDA PHARMACEUTICAL COMPANY LIMITED AND ULTRAGENYX PHARMACEUTICAL INC. JUNE 6, 2016

LICENSE AND COLLABORATIONAGREEMENT

This License and Collaboration Agreement (this "Agreement") is made as of the 6th day of June, 2016 (the "Execution Date") by and between **Takeda Pharmaceutical Company Limited**, a company incorporated under the laws of Japan having its principal place of business at 1-1, Doshomachi 4-chome, Chuo-ku, Osaka 540-8645, Japan ("Takeda"), and **Ultragenyx Pharmaceutical Inc.**, a company incorporated under the laws of California, having its principal place of business at 60 Leveroni Court, Novato, CA 94949, United States ("Ultragenyx"). Ultragenyx and Takeda are sometimes referred to herein individually as a "Party" and collectively as the "Parties."

RECITALS

WHEREAS, Takeda has developed certain compounds and products potentially applicable to rare genetic disease indications;

WHEREAS, Ultragenyx is a pharmaceutical company with significant experience with the development of products for rare genetic disease indications; and

WHEREAS, Ultragenyx and Takeda desire to establish a collaboration for the further development and commercialization of certain products potentially applicable to rare genetic disease and other indications.

NOW, THEREFORE, in consideration of the foregoing and the mutual agreements set forth below, and other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties agree as follows:

ARTICLE 1 – DEFINITIONS

1.1 "[***] Development Plans" has the meaning set forth in Section 4.3(b).

1.2 "[***] License Negotiation Period" has the meaning set forth in Section 5.1(a).

1.3 "[***] Option" has the meaning set forth in Section 5.1(a).

1.4 "[***] Option Term" has the meaning set forth in Section 5.1(a).

1.5 "[***] Patent Prosecution" has the meaning set forth in Section 12.3(a).

1.6 "[***] Compound" means [***].

1.7 "[***] Product" means any pharmaceutical product that contains a [***] Compound, including all forms, presentations, strengths, doses and formulations (including any method of delivery).

1.8 "[***] Research Plan" has the meaning set forth in Section 6.3(a).

1.9 "Accounting Standards" mean GAAP in the case of Ultragenyx and IFRS in the case of Takeda.

1.10 "Affiliate" means, with respect to a particular Party, a person, corporation, partnership, or other entity that controls, is controlled by or is under common control with such Party. For the purposes of this definition, the word "control" (including, with correlative meaning, the terms "controlled by" or "under the common control with") means the actual power, either directly or indirectly through one or more intermediaries, to direct or cause the direction of the management and policies of such entity, whether by the ownership of fifty percent (50%) or more of the voting stock of such entity, or by contract or otherwise.

1.11 "Agreement" has the meaning set forth in the preamble.

1.12 "Alliance Manager" means the person appointed by each Party from within their respective organization to coordinate and facilitate the communication, interaction and cooperation of the Parties pursuant to this Agreement.

1.13 "Applicable Laws" means all applicable statutes, ordinances, regulations, rules, or orders of any kind whatsoever of any Governmental Authority, including the U.S. Food, Drug and Cosmetic Act, (21 U.S.C. §301 et seq.) (the "FFDCA"), Prescription Drug Marketing Act, the Generic Drug Enforcement Act of 1992 (21 U.S.C. §335a et seq.), U.S. Patent Act (35 U.S.C. §1 et seq.), Federal Civil False Claims Act (31 U.S.C. §3729 et seq.), and the Anti-Kickback Statute (42 U.S.C. §1320a-7b et seq.), all as amended from time to time, together with any rules, regulations, and compliance guidance promulgated thereunder.

1.14 "Bankruptcy Laws" has the meaning set forth in Section 15.6(b).

1.15 "Bayh-Doyle Act" means the Patent and Trademark Law Amendments Act of 1980, as amended, codified at 35 U.S.C. §§ 200-212, as well as any regulations promulgated pursuant thereto, including 37 C.F.R. Part 401, and any successor statutes or regulations.

1.16 "[***] License Agreement" means the License Agreement by and between Ultragenyx and [***].

1.17 "Breaching Party" has the meaning set forth in Section 15.2(a).

1.18 "Bulk Drug Product" means a Product that has been Manufactured into a final pharmaceutical product, including drug substance (e.g., tablets or granules) for administration to humans in accordance with Applicable Laws, but has not been Packaged for use in Clinical Trials or for Commercialization.

1.19 "Business Day" means a day other than Saturday, Sunday or any other day on which commercial banks located in the State of New York, U.S., or Japan, are authorized or obligated by Applicable Laws to close.

1.20 "Calendar Quarter" means the respective periods of three (3) consecutive calendar months ending on March 31, June 30, September 30 and December 31; provided, however, that
(a) the first Calendar Quarter of the Term shall extend from the Effective Date to the end of the first complete Calendar Quarter thereafter; and (b) the last Calendar Quarter of the Term shall end upon the expiration or termination of this Agreement.

1.21 "Calendar Year" means the twelve-month period ending on December 31; provided however, that (a) the first Calendar Year of the Term, shall begin on the Effective Date and end on December 31, 2016; and (b) the last Calendar Year of the Term shall end on the date of expiration or termination of this Agreement.

1.22 "Candidate Product" has the meaning set forth in Section 6.2(a).

1.23 "Change of Control" of Ultragenyx means if: (a) any Third Party acquires directly or indirectly the beneficial ownership of any voting security of Ultragenyx, or if the percentage ownership of such person or entity in the voting securities of Ultragenyx is increased through stock redemption, cancellation or other recapitalization, and immediately after such acquisition or increase such Third Party is, directly or indirectly, the beneficial owner of voting securities representing [***] of the total voting power of all of the then- outstanding voting securities of Ultragenyx; (b) [***], which would result in stockholders or equity holders of Ultragenyx, or an Affiliate of Ultragenyx, immediately prior to such transaction [***] of the surviving entity (or its parent entity) immediately following such transaction; (c) the stockholders or equity holders of Ultragenyx approve [***], other than pursuant to the transaction as described above or to an Affiliate; or (d) the sale or other transfer to a Third Party of [***].

1.24 "Claim" has the meaning set forth in Section 17.1.

1.25 "Clinical Trial" means any human clinical study or trial of a pharmaceutical product in the Licensed Field in the Territory, including Phase I Trials, Phase II Trials, Phase III Trials and Phase IV Trials.

1.26 "Collaboration Activities" has the meaning set forth in Section 2.2(a).

1.27 "Collaboration Term" means (a) with respect to [***] from the Effective Date and (b) other than with respect to [***], unless, in case of each of the foregoing clauses (a) or (b), (i) extended by mutual agreement of the Parties, or (ii) terminated earlier in accordance with the terms of this

Agreement; provided that if at the expiration of the foregoing period, an Option Negotiation Period is then ongoing, the Collaboration Term with respect to such Option Product will automatically extend until the earlier of (A) expiration of such Option Negotiation Period or (B) execution of the applicable Option Product License Agreement.

1.28 "Combination Product" means a Product that is comprised of or contains a Compound as an active ingredient together with one (1) or more other active ingredients and is sold by a Party, or any of its Affiliates or sublicensees, either as a fixed dose or as separate doses as one (1) product.

1.29 "Commercialization" means all activities undertaken in support of the promotion, marketing, sale and distribution (including importing, exporting, transporting, customs clearance, warehousing, invoicing, handling and delivering the applicable Product to customers) of the applicable Product, including Manufacturing Product for commercial sale, sales force efforts, detailing, advertising, marketing, the creation and approval of Promotional Materials, sales and distribution, pricing, customer and government contracting, and medical affairs, including medical education, medical information, clinical science liaison activities, health economics and outcomes research, publications and investigator initiated research studies. "Commercialize" means to engage in Commercialization activities.

1.30 "Commercialization Plan" means, as applicable, (a) a plan prepared by Ultragenyx pursuant to Section 5.3 containing an overview of the general strategy and a high-level budget for the promoting and marketing of the Licensed Products in the Ultragenyx Field in the Territory or (b) a plan prepared by Takeda pursuant to Section 5.3 containing an overview of the general strategy for the promoting and marketing of the Licensed [***] Product in the Takeda Field in the Territory.

1.31 "Commercially Reasonable Efforts" means with respect to the efforts to be expended, or considerations to be undertaken, by a Party or its Affiliates with respect to any objective, activity or decision to be undertaken under this Agreement with respect to the Compounds or Products, the commercially reasonable efforts, expertise, and resources commonly used by such Party for a product owned by it or to which it has exclusive rights in the applicable territory, which, as compared with a Product, is of similar market potential, at a similar stage in its development or product life, and involves similar risks, all as measured based upon the facts and circumstances at the time such efforts are due, taking into account issues of: efficacy and safety, the competitiveness of alternative products sold by Third Parties, the product profile (including Labeling), the proprietary protection and regulatory exclusivity, the expected and actual profitability and return on investment, and all other similar relevant factors.

1.32 "Committee" has the meaning set forth in Section 2.3(a).

1.33 "Common Stock Purchase Agreement" means the common stock purchase agreement entered into on even date hereof by and between Ultragenyx and Takeda (or one of its Affiliates) providing for Takeda's (or one of its Affiliate's) purchase of common stock of Ultragenyx.

1.34 "Competing Product" means [***].

1.35 "Compound" means the Licensed [***] Compound, a Licensed Analog Compound, [***] Compound, Candidate Product or Ultragenyx Pipeline Compound, as applicable.

1.36 "Confidential Information" means all non-public or proprietary Information disclosed by a Party to the other Party under this Agreement, which may include ideas, inventions, discoveries, concepts, compounds, compositions, formulations, formulas, practices, procedures, processes, methods, knowledge, know-how, trade secrets, technology, inventories, machines, techniques, development and commercialization plans and related information, designs, drawings, computer programs, skill, experience, documents, apparatus, results, clinical and regulatory strategies, regulatory documentation, information and submissions pertaining to, or made in association with, filings with any Regulatory Authority, data, including pharmacological, toxicological and clinical data, analytical and quality control data, manufacturing data and descriptions, Patent and legal data, market data, financial data or descriptions, devices, assays, chemical formulations, specifications, material, product samples and other samples, physical, chemical and biological materials and compounds, and the like, without regard as to whether any of the foregoing is marked "confidential" or "proprietary," or disclosed in oral, written, graphic, or electronic form. Confidential Information shall include: (a) the terms and conditions of this Agreement; and (b) Confidential Information disclosed by either Party pursuant to the Confidentiality Agreement.

1.37 "Confidentiality Agreement" means the Mutual Confidential Disclosure Agreement dated March 13, 2015 by and between Takeda Pharmaceuticals International, Inc. and Ultragenyx Pharmaceutical Inc.

1.38 "Control" means, with respect to any Information, Patent, trademark or other intellectual property right, ownership or possession by a Party, including its Affiliates, of the ability (without taking into account any rights granted by one Party to the other Party under the terms of this Agreement) to grant access, a license or a sublicense to such Information, Patent, trademark or other intellectual property right without violating the terms of any agreement or other arrangement with, or necessitating the consent of, any Third Party, at such time that the Party would be first required under this Agreement to grant the other Party such access, license or sublicense.

1.39 "Cover", "Covering" or "Covered" means, with respect to a product, technology, process or method, that, in the absence of ownership of or a license granted under a Valid Claim, the practice or Exploitation of such product, technology, process or method would infringe such Valid Claim (or, in the case of a Valid Claim that has not yet issued, would infringe such Valid Claim if it were to issue).

1.40 "Cure Period" has the meaning set forth in Section 15.2(a).

1.41 "Data Package" means the Final [***] Data Package, Final Phase II Data Package or Final Phase III Data Package, as applicable.

1.42 "Development" means all non-clinical and clinical drug development activities, including toxicology, pharmacology, and other non-clinical efforts, statistical analysis, the performance of Clinical Trials, including the Manufacturing of the applicable Product for use in the Clinical Trials, or other activities necessary to obtain or maintain, Regulatory Approval of the applicable Products. "Development" shall exclude Commercialization activities. When used as a verb, "Develop" means to engage in Development activities.

1.43 "Disclosing Party" has the meaning set forth in Section 14.1.

1.44 "Dispute" has the meaning set forth in Section 16.1.

1.45 "Effective Date" means the date this Agreement becomes effective, as determined in accordance with Section 18.1.

1.46 "EMA" means the European Medicines Agency or any successor agency or authority having substantially the same function.

1.47 "EU" means all of the European Union member states as of the applicable time during the Term.

1.48 "Execution Date" has the meaning set forth in the preamble.

1.49 "Exercised Countries" has the meaning set forth in Section 8.2(c).

1.50 "Exercised Product License Agreement" has the meaning set forth in Section 8.2(d).

1.51 "Exercised Products" has the meaning set forth in Section 8.2(c).

1.52 "Expert" means a disinterested, conflict-of-interest-free individual who is neutral and independent of both Parties and all of their respective Affiliates and sublicensees and who, with respect to a dispute concerning a financial, commercial, scientific or regulatory matter, possesses appropriate expertise to resolve such dispute. Neither the Expert (nor any of the Expert's current or former employers) shall be or have been at any time, to the Knowledge of the Parties, an employee, officer, director or, during the previous five (5) years, a consultant or contractor of either Party or any of its Affiliates.

1.53 "Exploit" or "Exploitation" means to research, import, Manufacture, have Manufactured, export distribute, use, have used, sell, have sold, or offer for sale, including to Develop, Commercialize, register, modify, enhance, improve or otherwise dispose of.

1.54 "FDA" means the U.S. Food and Drug Administration, or any successor agency thereto.

1.55 "Final [***] Data Package" means all information the Parties agree that Ultragenyx shall provide to or give access to Takeda at the conclusion of the activities contemplated under the Initial [***] Development Plan for a given Licensed [***] Product as it relates to the Takeda Field, but which will include at a minimum (a) validated and reproducible tables, listings and graphs,
(b) all adverse event listings, safety narratives, CMC data and information, and applicable

Regulatory Documentation, (c) preclinical study results and final, if possible, or preliminary toxicology and pharmacology reports, and (d) a preliminary Phase I report and all Phase I clinical data.

1.56 "Final Phase II Data Package" means on a Product-by-Product basis, all Information the Parties agree that Ultragenyx shall provide to or give access to Takeda at the conclusion of a Phase II Clinical Trial and after database lock, but which will include at a minimum (a) validated and reproducible tables, listings and graphs, (b) all adverse event listings, safety narratives, CMC data and information, and applicable Regulatory Documentation, (c) final, if possible, or preliminary toxicology and pharmacology reports, (d) the Phase I final report and all Phase I clinical data, and (e) a preliminary Phase II report and all Phase II clinical data.

1.57 "Final Phase III Data Package" means, on a Product-by-Product basis, all Information the Parties agree that Ultragenyx shall provide to or give access to Takeda at the conclusion of a Phase III Clinical Trial and after database lock, but which will include at a minimum (a) validated and reproducible tables, listings and graphs, (b) all adverse event listings, material safety narratives, CMC data and information, and applicable Regulatory Documentation, (c) final, if possible, or preliminary toxicology and pharmacology reports, (d) the Phase I final report and all Phase I clinical data to the extent not previously provided to Takeda, (e) the Phase II final report and all Phase II clinical data to the extent not previously provided to Takeda, and (f) the preliminary Phase III report and all Phase III clinical data.

1.58 "Finished Product" means Bulk Drug Product that has been Packaged into a form suitable for use in Clinical Trials or for Commercial purposes (i.e., bottles or blisters), including samples, in accordance with Applicable Laws.

1.59 "First Commercial Sale" means, on a country-by-country basis, the first sale of a Product under this Agreement by a Party, its Affiliates or its sublicensees to an end user or prescriber for use, consumption or resale of the Product in a country in the applicable territory in the applicable field where Regulatory Approval of the Product has been obtained and where the sale results in a recordable Net Sale. Sale of a Product under this Agreement by a Party to an Affiliate or a sublicensee of such Party shall not constitute a First Commercial Sale unless such Affiliate or such sublicensee is the end user of such Product. Also, sale of a Product under this Agreement by a Party, its Affiliates or its sublicensees in a jurisdiction where Regulatory Approval for that Product has not yet been attained shall not constitute a First Commercial Sale under this Agreement.

1.60 Force Majeure" means any event beyond the reasonable control of the affected Party including: embargoes; war or acts of war, including terrorism; insurrections, riots, or civil unrest; strikes, lockouts or other labor disturbances; epidemics, fire, floods, earthquakes or other acts of nature; or acts, omissions or delays in acting by any governmental authority (including the refusal of the competent government agencies to issue required Regulatory Approvals due to reasons other than the affected Party's negligence or willful misconduct or any other cause within the reasonable control of the affected Party), and failure of plant or machinery (provided that such failure could not have been prevented by the exercise of skill, diligence, and prudence

that would be reasonably and ordinarily expected from a skilled and experienced person engaged in the same type of undertaking under the same or similar circumstances).

1.61 "FTE" means eighteen hundred (1800) hours of work per full Calendar Year (or equivalent pro-rata portion thereof for a period less than twelve (12) months) devoted to or in support of the Development of the applicable Products in accordance with the Research Plans or the Manufacturing of a Product or the provision of Research Support (but excluding, for clarity, time spent travelling to and attending meetings under this Agreement and scientific and medical conferences), that is carried out by one or more qualified scientific or technical employees or contract personnel of Takeda or its Affiliates, as such hours are measured in accordance with Takeda's normal time allocation practices. For the avoidance of doubt, FTE only applies to employees of a Party, and does not apply to contractors of Takeda.

1.62 "FTE Cost" means, for any period, the FTE Rate multiplied by the number of FTEs in such period.

1.63 "FTE Rate" means a rate of [***] per FTE per Calendar Year (pro-rated for the period beginning on the Effective Date and ending at the end of the first Calendar Year) for personnel engaged in Development activities. Such rate shall be adjusted annually, with each annual adjustment effective as of January 1 of each calendar year (with the first such annual adjustment to be made as of January 1, 2018) to correspond with the total percentage change in the Consumer Price Index for All Urban Consumers (CPI-U) for the U.S. City Average, 1982-84 = 100, calculated by the U.S. Bureau of Labor Statistics over the twelve (12)-month period preceding each such January 1.

1.64 "GAAP" means generally accepted accounting principles current in the U.S.

1.65 "Generic Competition Percentage" means, with respect to any Product in a given country in the Territory or Takeda Territory (as applicable), all units of the Generic Product(s) for such Product, sold in the aggregate in such country divided by the sum of: (a) all units of the Product sold in such country, and (b) all units of the Generic Product(s) sold in the aggregate in such country, where, in each case, the number of units of a Product and each Generic Product sold shall be based on the average of the monthly IMS data (or IMS-equivalent data if IMS data are not available).

1.66 "Generic Product" means, on a Product-by-Product and country-by-country basis, any pharmaceutical product sold by a Third Party, other than as a sublicensee to this Agreement that:
(a) contains the same active ingredients as the applicable Product, in the same dosage form (e.g., oral) as the applicable Product; or (b) is A/B Rated with respect to such Product or otherwise approved by the Regulatory Authority in such country as a substitutable generic for such Product; or (c) is approved in the applicable field by a Regulatory Authority pursuant to an NDA filed by a Third Party under Section 505(b)(2) or 505(j)(2) of the FFDCA (or an equivalent Regulatory Approval Application filed outside the U.S.), contains the active ingredients in the Product, and relies on the finding of safety and/or effectiveness in the Regulatory Approval of the Product. For the purposes of this definition, "A/B Rated" means, inside the U.S., "therapeutically equivalent" as determined by the FDA, applying the definition of

"therapeutically equivalent" set forth in the preface to the then-current edition of the FDA publication "Approved Drug Products With Therapeutic Equivalence Evaluations and, outside the U.S., such equivalent determination by the applicable Regulatory Authorities as is necessary to permit pharmacists or other individuals authorized to dispense pharmaceuticals under Applicable Law to substitute one product for another product in the absence of specific instruction from a physician or other authorized prescriber under Applicable Law."

1.67 "Good Clinical Practices", "GCP" or "cGCP" means the then-current standards, practices and procedures promulgated or endorsed by the FDA as set forth in the guidelines adopted by the International Conference on Harmonization ("ICH"), titled "Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance," (or any successor document) including related regulatory requirements imposed by the FDA and comparable regulatory standards, practices and procedures promulgated by the EMA, PMDA or other Regulatory Authority applicable to the Territory, as they may be updated from time to time.

1.68 "Good Laboratory Practices", "GLP", or "cGLP" means the then-current standards, practices and procedures promulgated or endorsed by the FDA as set forth in 21 C.F.R. Part 58 (or any successor statute or regulation), including related regulatory requirements imposed by the FDA and comparable regulatory standards, practices and procedures promulgated by the EMA, PMDA or other Regulatory Authority applicable to the Territory, as they may be updated from time to time, including applicable guidelines promulgated under the ICH.

1.69 "Good Manufacturing Practices", "GMP", or "cGMP" means the then-current good manufacturing practices required by the FDA, as set forth in the FFDCA, as amended, and the regulations promulgated thereunder, for the manufacture and testing of pharmaceutical materials, and comparable Applicable Law related to the manufacture and testing of pharmaceutical materials in jurisdictions outside the U.S., including the quality guideline promulgated by the ICH designated ICH Q7A, titled "Q7A Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients" and the regulations promulgated thereunder, in each case as they may be updated from time to time.

1.70 "Governmental Authority" means any multi-national, federal, state, local, municipal or other government authority of any nature (including any governmental division, subdivision, department, agency, bureau, branch, office, commission, council, court or other tribunal).

1.71 "Hatch-Waxman Act" means the Drug Price Competition and Patent Term Restoration Act, 21 U.S.C. 355, as amended

1.72 "House Mark" means the trademark that a Party uses to identify its commercial operations.

1.73 "HSR Act" means the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended, and the rules promulgated thereunder.

1.74 "HSR Conditions" means the following conditions, collectively: (a) the waiting period under the HSR Act shall have expired or earlier been terminated; (b) no injunction (whether

temporary, preliminary or permanent) prohibiting consummation of the transaction contemplated by this Agreement or any material portion hereof shall be in effect; (c) no judicial or administrative proceeding opposing consummation of all or any part of this Agreement shall be pending; and (d) no requirements or conditions shall have been imposed by the United States Department of Justice or Federal Trade Commission (as applicable) in connection with the filings by the Parties under the HSR Act, other than requirements or conditions that are satisfactory to the Party on whom such requirements or conditions are imposed.

1.75 "HSR Filing" means filings with the United States Federal Trade Commission and the Antitrust Division of the United States Department of Justice of a Notification and Report Form for Certain Mergers and Acquisitions (as that term is defined in the HSR Act) with respect to the subject matter of this Agreement, together with all required documentary attachments thereto.

1.76 "IFRS" means the International Financial Reporting Standards as promulgated by the International Standards Accounting Board and as they may be updated for time to time.

1.77 "IND" means an Investigational New Drug application as defined in the FFDCA, as amended, and applicable regulations promulgated hereunder by the FDA, or a clinical trial authorization application for a product filed with a Regulatory Authority in any other regulatory jurisdiction outside the U.S., the filing of which is necessary to commence or conduct clinical testing of a pharmaceutical product in humans in such jurisdiction.

1.78 "IND Date" means the date on which ownership of Product INDs is transferred or a right of reference is granted pursuant to Section 9.2(a)(i), in the case of transfers or grants to Ultragenyx, or pursuant to Section 9.2(b)(i), in the case of transfers to Takeda..

1.79 "Indemnifying Party" has the meaning set forth in Section 17.3(a).

1.80 "Indemnitee" has the meaning set forth in Section 17.3(a).

1.81 "Information" means information, Inventions, discoveries, compounds, compositions, formulations, formulas, practices, procedures, processes, methods, knowledge, trade secrets, technology, techniques, designs, drawings, correspondence, computer programs, documents, apparatus, results, strategies, regulatory documentation, information and submissions pertaining to, or made in association with, filings with any Regulatory Authority or patent office, data, including pharmacological, toxicological, non-clinical and clinical data, analytical and quality control data, manufacturing data and descriptions, market data, financial data or descriptions, devices, assays, chemical formulations, specifications, material, product samples and other samples, physical, chemical and biological materials and compounds, and the like, in written, electronic, oral or other tangible or intangible form, now known or hereafter developed, whether or not patentable.

1.82 "Initial [***] Development Plan" means the plan (including timeline and budget) covering preliminary Development activities to be completed by Ultragenyx and Takeda (to the extent expressly provided in such plan) for a Licensed [***] Product in the Licensed Field attached

hereto as Exhibit 1.82, as such plan may be amended from time to time pursuant to Section 2.1(a)(v).

1.83 "Inventions" means any and all inventions, discoveries and developments, whether or not patentable, made, conceived or reduced to practice in the course of performance of this Agreement, whether made, conceived or reduced to practice solely by, or on behalf of, Takeda, Ultragenyx, the Parties jointly, or any Affiliate of the same.

1.84 "Joint Know-How" means all Information included in the Joint Inventions.

1.85 "Joint Intellectual Property" means, collectively, Joint Know-How and Joint Patents.

1.86 "Joint Invention" has the meaning set forth in Section 12.1(b).

1.87 "Joint Patents" has the meaning set forth in Section 12.3(c).

1.88 "Joint Research Committee" or "JRC" has the meaning set forth in Section 2.2(a).

1.89 "Joint Steering Committee" or "JSC" has the meaning set forth in Section 2.1(a).

1.90 "Knowledge" means, as applied to a Party, that such Party shall be deemed to have knowledge of a particular fact or other matter to the extent that a person within the Knowledge Group knew of such fact or other matter.

1.91 "Knowledge Group" means, with respect to each Party, the individuals holding the positions listed on Exhibit 1.91; provided that if one or more of the individuals listed on Exhibit
1.191 no longer holds the same position or title set forth opposite his/her name, (a) such person shall continue to be considered part of the Knowledge Group, and (b) his/her replacement shall also be considered part of the Knowledge Group.

1.92 "Labeling" means the healthcare professional information or patient information used in the Territory that is part of the Product Regulatory Approval including the package insert, medication guides, company core safety information (CCSI) and company core data sheet (CCDS).

1.93 "Lead Regulatory Party" has the meaning set forth in Section 9.1.

1.94 "Licensed [***] Compound" means [***] as further described on, and with the chemical structure set forth in, Exhibit 1.94.

1.95 "Licensed [***] Know-How" means Information related to the (a) Licensed [***] Compound, Controlled by Takeda as of the Execution Date or during the Term, and/or (b) Licensed Analog Compound specified in the Agreement Controlled by Takeda as of the Execution Date, in each case including data, reports, and materials related to preclinical studies, regulatory filings/correspondence, and chemistry, manufacturing and controls and necessary or

reasonably useful for the Exploitation of a Licensed [***] Compound or a Licensed Analog Compound.

1.96 "Licensed [***] Patent" means the Patent that is Controlled by Takeda as of the Execution Date identified as the Licensed [***] Patent on Exhibit 1.168, and all Patents Controlled by Takeda during the Term that claim priority to such Patent.

1.97 "Licensed [***] Product" means any pharmaceutical product that contains the Licensed [***] Compound, including all forms, presentations, strengths, doses and formulations (including any method of delivery).

1.98 "Licensed [***] Technology" means the Licensed [***] Patent and Licensed [***] Know- How.

1.99 "Licensed Analog Compounds" means (a) the compounds with the chemical structures listed on Exhibit 1.99 and (b) any structures defined by [***] where approved by the JSC pursuant to Section 2.1(a)(iii)) [***], that are disclosed in the Licensed [***] Patent and that are developed pursuant to, and as specified in, a mutually agreed research plan conducted by Ultragenyx involving modifications to such structures. Exhibit 1.99 shall be updated from time to time to include those chemical structures described in the foregoing subclause (b).

1.100 "Licensed Analog Product" means any pharmaceutical product that contains a Licensed Analog Compound, including all forms, presentations, strengths, doses and formulations (including any method of delivery).

1.101 "Licensed Field" means [***].

1.102 "Licensed Option Product" means any Option Product for which the Parties have executed an Option Product License Agreement.

1.103 "Licensed Product" means the Licensed [***] Products and Licensed Analog Products, as applicable.

1.104 "Licensed Product Improvement" means any Invention related to the Licensed [***] Compound, Licensed Analog Compounds, or Licensed Products made (a) solely by, or on behalf of, Ultragenyx or its Affiliates or sublicensees under this Agreement or (b) solely by Takeda or its Affiliates under this Agreement. For clarity, (i) employees of Ultragenyx or its Affiliates or sublicensees, or their respective agents or independent contractors receiving consideration from Ultragenyx or its Affiliates or sublicensees in the course of conducting activities under this Agreement, shall be considered "solely by, or on behalf of" pursuant to this Section 1.104, and (ii) neither Takeda nor any of its Affiliates shall, under any circumstances under this Agreement, be considered an agent or independent contractor of Ultragenyx or any of its Affiliates or sublicensees for purposes of this Section 1.104.

1.105 "Licensed Product Improvement Patents" means Patents that Cover Licensed Product Improvements that do not claim priority (in accordance with Section 1.129) to the Licensed [***] Patent.

1.106 "Licensed Product Royalty Term" means, on a country-by-country and Licensed Product- by-Licensed Product basis, the period commencing on the First Commercial Sale of such Licensed Product in such country in the Territory and ending upon the later of (a) [***] years after First Commercial Sale of such Licensed Product in such country, (b) the expiration in such country of the last Valid Claim from the Licensed [***] Patent that Covers the composition, or method of making or using, such Licensed Product, or (c) the expiration of the applicable Regulatory Exclusivity of a Licensed Product.

1.107 "Listed Compounds" has the meaning set forth in Section 6.1.

1.108 "Loss" has the meaning set forth in Section 17.1.

1.109 "Marketing Authorization Application" or "MAA" means an application for Regulatory Approval (but excluding Pricing Approval) in any particular jurisdiction other than the U.S.

1.110 "Manufacture" means all activities related to the manufacturing of a Finished Product or Bulk Drug Product, including the manufacture of any ingredient used therein, for Development or Commercialization in the Territory, packaging, in-process and Product testing, validation, release of Product or any component or ingredient thereof, quality assurance activities related to manufacturing and release of Product, ongoing stability tests, Packaging of Bulk Drug Product into Finished Product and regulatory activities related to any of the foregoing.

1.111 "NDA" means a New Drug Application or supplemental New Drug Application as contemplated by Section 505(b) of the FFDCA, as amended, and the regulations promulgated thereunder, submitted to the FDA pursuant to Part 314 of Title 21 of the U.S. Code of Federal Regulations, including any amendments thereto.

1.112 "Net Sales" means, with respect to any Product and calculated in accordance with Accounting Standards consistently applied across Products, the gross revenue recognized by a Party, its Affiliates and sublicensees for sales of such Product to Third Parties, less the following deductions, to the extent such deductions are paid, incurred or otherwise taken, reasonable and customary, provided to Third Parties, and actually allowed with respect to such sales:

(a) reasonable cash, trade or quantity discounts, charge-back payments, and rebates actually granted to trade customers, managed health care organizations, pharmaceutical benefit managers, group purchasing organizations and national, state, or local government; and

(b) credits, rebates or allowances actually allowed upon prompt payment or on account of claims, damaged goods, rejections or returns of such Product, including in connection with recalls, and the actual amount of any write-offs for bad debt (not to exceed one percent (1%)) (provided that an amount subsequently recovered will be treated as Net Sales)

(c) inventory management fees and costs of freight, carrier insurance, and other transportation charges directly related to the distribution of such Product; and

(d) taxes, duties or other governmental charges (including (i) any tax such as a value added or similar tax, other than any taxes based on income, and (ii) any payments made to the Pharmaceutical and Medical Device Agency ("*Kiko*") based on Section 19 or 22 of the "Act on Pharmaceuticals and Medical Devices Agency (Act No.192 of 2002)") directly levied on or measured by the billing amount for such Product, as adjusted for rebates and refunds.

Notwithstanding the foregoing, amounts received or invoiced by a Party, its Affiliates or sublicensees for the sale of such Product among a Party, its Affiliates or sublicensees for resale shall not be included in the computation of Net Sales hereunder. In any event, any amounts received or invoiced by a Party, its Affiliates and sublicensees shall be accounted for only once. For purposes of determining Net Sales, a Product shall be deemed to be sold when the revenue generated from such sale is recognized in accordance with the Accounting Standards. Each Party shall record such Net Sales as the "principal" and not the "agent" as defined under the Accounting Standards. For clarity, a particular deduction may only be accounted for once in the calculation of Net Sales and no deductions may be made for the annual fee on prescription drug manufacturers imposed by the Patient Protection and Affordable Care Act, Pub. L. No. 111-148 (as amended). Net Sales shall exclude any samples of a Product transferred or disposed of at no cost for promotional, Development or educational purposes.

The Net Sales of any Combination Product:

(i) for which the Product(s) and other active ingredient(s) of such Combination Product are sold separately by a Party, or any of its Affiliates or sublicensees, in such country, then Net Sales for such Combination Product in such country shall be calculated by multiplying actual Net Sales of such Combination Product in such country by the fraction A/(A+B), where A is the average Net Sales price of the Product as the only active ingredient(s), as sold separately by a Party or any of its Affiliates or sublicensees in such country, and B is the average net sales (calculated in a manner analogous to the manner in which Net Sales are calculated as set forth above) price of the other active ingredient(s) in the Combination Product as sold separately by a Party or any of its Affiliates or sublicensees in such country;

(ii) for which the (A) Licensed Product of such Combination Product is/are sold separately by a Party or any of its Affiliates or sublicensees in such country and (B) the other active ingredient(s) in the Combination Product is/are not sold separately by a Party or any of its Affiliates or sublicensees in such country, then Net Sales for such Combination Product in such country shall be calculated by multiplying actual Net Sales of such Combination Product in such country by the fraction A/D, where A is the average Net Sales price of the Licensed Product as the only active ingredient(s), as sold separately by a Party or any of its Affiliates or sublicensees in such country, and D is the average Net Sales price of the Combination Product as sold separately by a Party or any of its Affiliates or sublicensees in such country; and

(iii) for which neither clause (i) nor clause (ii) above is applicable, the Parties shall determine Net Sales for such Combination Product in such country by mutual agreement

based on the relative contribution of the Licensed Product and the other active ingredient(s) in the Combination Product.

1.113 "Neutral Expert" has the meaning set forth in Section 16.3(a).

1.114 "Non-breaching Party" has the meaning set forth in Section 15.2(a).

1.115 "Notice Date" has the meaning set forth in Section 16.3(a).

1.116 "Option Negotiation Period" has the meaning set forth in Section 6.12(a).

1.117 "Option Notice" has the meaning set forth in Section 6.12(a).

1.118 "Option Product" means (a) a Candidate Product selected pursuant to Section 6.10 or (b) a [***] Product, as applicable.

1.119 "Option Product Improvements" means any Invention related to a [***] Product or another Research Product made (a) solely by, or on behalf of, Ultragenyx or its Affiliates or sublicensees under this Agreement, or (b) solely by Takeda or its Affiliates under this Agreement. For clarity,
(i) employees of Ultragenyx or its Affiliates or sublicensees, or their respective agents or independent contractors receiving consideration from Ultragenyx or its Affiliates or sublicensees in the course of conducting activities under this Agreement, shall be considered "solely by, or on behalf of" pursuant to this Section 1.119, and (ii) neither Takeda nor any of its Affiliates shall, under any circumstances under this Agreement, be considered an agent or independent contractor of Ultragenyx or any of its Affiliates or sublicensees for purposes of this Section 1.119.

1.120 "Option Product Improvement Patents" means Patents Covering Option Product Improvements.

1.121 "Option Product Key Terms" has the meaning set forth in Section 6.10(a).

1.122 "Option Product Know-How" means all Information Controlled by Takeda as of the Execution Date and during the Term that is necessary or reasonably useful for, as applicable, (a) Ultragenyx to evaluate whether to exercise the Ultragenyx Option or (b) Ultragenyx to Exploit an Option Product solely in accordance with the activities to be performed by Ultragenyx or its Affiliates or sublicensees under the Option Product Research Plan.

1.123 "Option Product License Agreement" has the meaning set forth in Section 6.12(a).

1.124 "Option Product Patents" means all Patents Controlled by Takeda as of the Execution Date and during the Term that are necessary or reasonably useful for the Exploitation of the Option Product(s) in the Ultragenyx Field in the Territory.

1.125 "Option Product Research Plan" has the meaning set forth in Section 6.10(a).

1.126 "Option Product Technology" means the Option Product Patents and Option Product Know-How.

1.127 "Packaging" means all activities related to the preparation of Bulk Drug Product into Finished Product, including application of the approved Labeling. "Packaged" means that Bulk Drug Product has been subject to complete Packaging.

1.128 "Party" has the meaning set forth in the preamble.

1.129 "Patents" means all patents, including any utility or design patent, and all applications thereof, including any provisional application, whether in the Territory or any other jurisdiction; any other patent or patent application claiming priority to (a) any such specified patent or patent application or (b) any patent or patent application from which such specified patent or patent application claim priority; and (c) all divisionals, continuations, continuations in-part, registrations, reissues, re-examinations, renewals, supplemental protection certificates, or extensions of (a) or (b).

1.130 "Patent Term Extension" means any term extensions, supplementary protection certificates and equivalents thereof offering Patent protection beyond the initial term with respect to any issued Patents.

1.131 "Person" means an individual, sole proprietorship, partnership, limited partnership, limited liability partnership, corporation, limited liability company, business trust, joint stock company, trust, incorporated association, joint venture or similar entity or organization, including a government or political subdivision, department or agency of a government.

1.132 "Phase I Trial" means a clinical trial of a Product with the endpoint of determining initial tolerance, safety, pharmacokinetic or pharmacodynamic information in single dose, single ascending dose, multiple dose and/or multiple ascending dose regimens.

1.133 "Phase II Trial" means a clinical trial of a Product on patients, including possibly pharmacokinetic, pharmacodynamic and dose-ranging studies, the principal purposes of which are to make a preliminary determination that such product is safe for its intended use and to obtain sufficient information about such product's efficacy or dose-response information to permit the design of further clinical trials.

1.134 "Phase III Trial" means a pivotal clinical trial of a Product on a sufficient number of patients, which trial is designed to (a) establish that a product is safe and efficacious for its intended use; (b) define warnings, precautions and adverse reactions that are associated with the product in the dosage range to be prescribed; and (c) pivotal to support submission of a Regulatory Approval Application for such product.

1.135 "Phase IV Trial" means a clinical trial of a Product, including pharmacokinetic studies, which trial (a) is not required in order to obtain Regulatory Approval of an indication; and (b) either (i) is required by the Regulatory Authority as mandatory to be conducted on or after the Regulatory Approval of an indication, or (ii) is conducted voluntarily to enhance marketing or scientific knowledge of the product (e.g., providing additional drug profile, outcomes research, safety data or marketing support information, or supporting expansion of product labeling).

1.136 "PMDA" means Japan's Pharmaceuticals and Medical Devices Agency and any successor agency(ies) or authority having substantially the same function.

1.137 "Preexisting Third Party IP" means those intellectual property rights owned or controlled by Third Parties as of the Execution Date that are necessary or reasonably useful for the Exploitation of Licensed Products and which are set forth in Exhibit 1.137.

1.138 "Pricing Approval" means governmental approval, agreement, determination or decision establishing prices that can be charged and/or reimbursed for a Product in a jurisdiction where the applicable Governmental Authority or Regulatory Authority approves or determines the pricing of pharmaceutical products.

1.139 "Product" means any Licensed [***] Product, Licensed Analog Product, Licensed Option Product or Ultragenyx Pipeline Product, as applicable.

1.140 "Product Complaint" means all data, which come to the attention of either Party, its Affiliates or its sub-licensees, concerning any dissatisfaction regarding a Product of such a nature and magnitude that it is required under Applicable Laws to be collected, maintained and reported to a Regulatory Authority, including reports of actual or suspected product tampering, contamination, mislabeling or inclusion of improper ingredients.

1.141 "Product IND" means any IND filed in the Territory related to a Product, whether in existence as of the Effective Date or filed with the FDA during the Term, including any supplements or amendments thereto. The Product INDs as of the Execution Date are set forth on Exhibit 1.141.

1.142 "Product Liabilities" means all losses, damages, fees, costs and other liabilities incurred by a Party, its Affiliate or its sublicensee and resulting from or relating to the any use of a Compound and/or a Product in a human (including in Clinical Trials and/or pursuant to Commercialization) in the Territory, other than any losses, damages, fees, costs and other liabilities that are a result of a Party's, its Affiliates' or its sublicensee's negligence, willful misconduct or breach of such Party's representations and warranties made hereunder. For the avoidance of doubt, Product Liabilities include, reasonable attorneys' and experts' fees and costs relating to any claim or potential claim against a Party, its Affiliate, or its sublicensee and all losses, damages, fees, costs. Product Liabilities shall not include liabilities associated with recalls and/or the voluntary or involuntary withdrawal of the Compound and/or a Product.

1.143 "Promotional Materials" means all written, printed, graphic, electronic, audio or video presentations of information, including journal advertisements, sales visual aids, formulary binders, reprints, direct mail, direct-to-consumer advertising, disease awareness materials, internet postings, broadcast advertisements and sales reminder aides (for example, note pads, pens and other such items, if appropriate) intended for use or used by or on behalf of a Party, its Affiliates or its sublicensees in connection with the Commercialization of a Product in the Territory.

1.144 "Product Regulatory Approval" means any Regulatory Documentation filed in the Territory which is related to a Product in the Licensed Field, whether in existence as of the Effective Date or filed with the applicable Regulatory Authority during the Term, including any supplements or amendments thereto.

1.145 "Product Trademarks" has the meaning set forth in Section 5.5(a).

1.146 "PVA" has the meaning set forth in Section 9.8(a)(i).

1.147 "Receiving Party" has the meaning set forth in Section 14.1.

1.148 "Regulatory Approval" means any approval or authorization, including Pricing Approvals, of any Regulatory Authority that is necessary for the Manufacture, use, storage, import, transport and/or sale of a Product in accordance with Applicable Laws.

1.149 "Regulatory Approval Application" means an NDA or BLA, or any corresponding application for Regulatory Approval in the Territory, including: (a) with respect to the European Union, an MAA filed with the EMA pursuant to the Centralized Approval Procedure or with the applicable Regulatory Authority of a country in Europe with respect to the decentralized procedure, mutual recognition or any national approval procedure; and (b) an MAA filed with the PMDA, including, in each case, all supplements, amendments, variations, extensions and renewals thereof.

1.150 "Regulatory Authority" means any applicable Governmental Authority involved in granting Regulatory Approval in a country or jurisdiction in the Territory, including in the U.S., the FDA and any other applicable Governmental Authority in the U.S. having jurisdiction over a Product; in the EU, the EMA or any competent Government Authority in the EU; in Japan, the PMDA; and any other applicable Governmental Authority having jurisdiction over a Product.

1.151 "Regulatory Documentation" means, with respect to each Research Product or Licensed Product, all: (a) Regulatory Materials, including all data contained therein and all supporting documents created for, submitted to or received from an applicable governmental agency or Regulatory Authority relating to such Regulatory Materials; and (b) other documentation or Information Controlled by a Party which is necessary or reasonably useful in order to Exploit such Product in the applicable Field in the Territory, including any registrations and licenses, regulatory drug lists, advertising and promotion documents shared with Regulatory Authorities, adverse event files, complaint files and Manufacturing records.

1.152 "Regulatory Exclusivity" means any exclusive marketing rights or data protection or other exclusivity rights conferred by any Regulatory Authority with respect to a Product in a country or jurisdiction in the Territory, other than a Patent right, including orphan drug exclusivity, pediatric exclusivity, rights conferred in the U.S. under the Hatch Waxman Act, in the EU under Directive 2001/83/EC, as amended, and Regulation (EC) No. 1901/2006, as amended, or in the Biologics Price Competition Act as set forth in the Patient Protection & Affordable Care Act, or rights similar thereto in other countries or regulatory jurisdictions in the Territory.

1.153 "Regulatory Materials" means, with respect to each Product, all documentation, correspondence, submissions and notifications submitted to or received from a Regulatory Authority that are necessary or reasonably useful in order to Exploit such Product in the applicable field in the Territory. For the avoidance of doubt, Regulatory Materials shall include, with respect to each Product, all INDs, Regulatory Approval Applications, Regulatory Approvals, Pricing Approvals and amendments and supplements for any of the foregoing, as well as the contents of any minutes from meetings (whether in person or by audio conference or videoconference) with a Regulatory Authority.

1.154 "Representative Expert" has the meaning set forth in Section 16.3(b).

1.155 "Research Materials" has the meaning set forth in Section 6.6(a).

1.156 "Research Plan" means a [***] Research Plan or Option Product Research Plan, as applicable.

1.157 "Research Product" means a [***] Product, Candidate Product or Option Product, as applicable.

1.158 "Research Support" has the meaning set forth in Section 7.1.

1.159 "Senior Officer" means the Head of Research & Development or his or her designee, in the case of Takeda and, the Chief Executive Officer or his or her designee, in the case of Ultragenyx.

1.160 "Takeda [***] License" means the licenses granted to Takeda in Section 3.2.

1.161 "Takeda Field" means [***].

1.162 "Takeda Indemnitee" has the meaning set forth in Section 17.1.

1.163 "Takeda Option" has the meaning set forth in Section 8.1.

1.164 "Takeda Option Field" means all human indications other than the Takeda Field for Licensed [***] Products, and all human indications for Licensed Analog Products, Licensed Option Products and Ultragenyx Pipeline Products.

1.165 "Takeda Option Negotiation Period" has the meaning set forth in Section 8.2(d).

1.166 "Takeda Option Notice" has the meaning set forth in Section 8.2(c).

1.167 "Takeda Option Term" means the period beginning on the Effective Date and ending on the earlier of (a) [***] after the Effective Date or (b) with respect to a Licensed [***] Product, Licensed Analog Product, Licensed Option Product, or Ultragenyx Pipeline Product, as

the case may be: (i) [***] after Takeda's receipt of the applicable Final Phase II Data Package for the applicable Licensed [***] Product, Licensed Analog Product or Licensed Option Product, (ii) [***] after Takeda's receipt of the Final Phase II Data Package (or Final Phase III Data Package in the case of [***]) for the applicable Ultragenyx Pipeline Product (other than [***]) and (iii) [***] after Takeda's receipt of the Final Phase II Data Package for [***]. Notwithstanding the foregoing, (a) in the event of a [***] of Ultragenyx [***], the Takeda Option Term will expire with respect to all applicable products (i.e., any Licensed [***] Product, Licensed Analog Product, Licensed Option Product, or Ultragenyx Pipeline Product) [***]; and (b) in the event of a [***] of Ultragenyx at any time [***], the Takeda Option Term will expire with respect to all applicable products (i.e., any Licensed [***] Product, Licensed Analog Product, Licensed Option Product, or Ultragenyx Pipeline Product) [***] after the closing of such [***].

1.168 "Takeda Patents" means the Licensed [***] Patent and any Patent that claims priority (in accordance with Section 1.129) to the Licensed [***] Patent during the Term, and the Ultragenyx Pipeline Improvement Patents Controlled by Takeda or its Affiliates. The Takeda Patents as of the Execution Date are set forth on Exhibit 1.168.

1.169 "Takeda Product Infringement" has the meaning set forth in Section 12.6(b)(i).

1.170 "Takeda ROFN Territory" means Japan.

1.171 "Takeda Royalty Term" means, on a country-by-country and Exercised Product-by- Exercised Product basis, the period commencing on the First Commercial Sale of such Exercised Product in a country in the Takeda Territory by Takeda, its Affiliates, or sublicensees that occurs after Takeda's exercise of the Takeda Option and ending upon the later of [***].

1.172 "Takeda Territory" means, (i) with respect to Licensed Products and Licensed Option Products, Japan and Asia and (ii) with respect Ultragenyx Pipeline Products, Japan.

1.173 "Tax Conditions" means, with respect to the premium being paid by Takeda to Ultragenyx under the Common Stock Purchase Agreement, Ultragenyx's confirmation of receipt of the tax residence certificate (IRS Form 6166) from the U.S. Internal Revenue Service specified in Section 11.11(c) and appropriate submission of such certificate and required forms and information with the Osaka Regional Taxation Bureau.

1.174 "Term" has the meaning set forth in Section 15.1.

1.175 "Terminated Product" means any: (a) Option Product for which an Option Product License Agreement has not been executed during the Option Negotiation Period in accordance with Section 6.12(a); (b) Research Product terminated pursuant to Section 6.7(d) or 18.5; (c) Licensed [***] Compound or Licensed [***] Product that reverts to Takeda pursuant to Section 4.3(f); or (d) Licensed Product or Research Product terminated pursuant to Section 15.2, 15.4 or 15.5.

1.176 "Territory" means worldwide.

1.177 "Third Party" means a Person other than Takeda and Ultragenyx and their respective Affiliates.

1.178 "Ultragenyx [***] Know-How" means all Information related to the Licensed [***] Compound Controlled by Ultragenyx during the Term.

1.179 "Ultragenyx [***] License" means the licenses granted to Ultragenyx in Section 3.1.

1.180 "Ultragenyx [***] Patents" means all Patents Controlled by Ultragenyx or its Affiliates as of the Execution Date or during the Term that are necessary or reasonably useful for the Exploitation of the Licensed [***] Compound or Licensed Analog Compound in the Licensed Field in the Territory, but expressly excluding any Licensed Product Improvement Patents. The Ultragenyx [***] Patents as of the Execution Date are set forth on Exhibit 1.188.

1.181 "Ultragenyx [***] Technology" means the Ultragenyx [***] Patents and Ultragenyx [***] Know-How.

1.182 "Ultragenyx Field" means the Licensed Field, excluding the Takeda Field.

1.183 "Ultragenyx In-License Agreement" means [***] and (g) any other applicable agreement between Ultragenyx (or its Affiliates) and a Third Party under which Takeda is granted a sublicense or other right under this Agreement.

1.184 "Ultragenyx Indemnitee" has the meaning set forth in Section 17.2.

1.185 "Ultragenyx Know-How" means all Information Controlled by Ultragenyx during the Term that is necessary or reasonably useful to Exploit a Compound or a Product in the Licensed Field.

1.186 "Ultragenyx Intellectual Property" means, collectively, Ultragenyx Know-How and Ultragenyx Patents.

1.187 "Ultragenyx Option" has the meaning set forth in Section 6.11.

1.188 "Ultragenyx Patents" means all Ultragenyx [***] Patents, Licensed Product Improvement Patents Controlled by Ultragenyx or its Affiliates, Option Product Improvement Patents Controlled by Ultragenyx or its Affiliates and Ultragenyx Pipeline Patents. The Ultragenyx Patents as of the Execution Date are set forth on Exhibit 1.188.

1.189 "Ultragenyx Pipeline Compound" means the active ingredient in an Ultragenyx Pipeline Product.

1.190 "Ultragenyx Pipeline Improvements" means any Invention related to an Ultragenyx Pipeline Product made (a) solely by, or on behalf of, Takeda or its Affiliates or sublicensees under this Agreement or (b) solely by Ultragenyx or its Affiliates under this Agreement. For clarity, (i) employees of Takeda or its Affiliates or sublicensees, or their respective agents or independent contractors receiving consideration from Takeda or its Affiliates or sublicensees in the course of conducting activities under this Agreement, shall be considered "solely by, or on behalf of" pursuant to this Section 1.190, and (ii) neither Ultragenyx nor any of its Affiliates shall, under any circumstances under this Agreement, be considered an agent or independent contractor of Takeda or any of its Affiliates or sublicensees for purposes of this Section 1.190.

1.191 "Ultragenyx Pipeline Improvement Patents" means Patents that Cover Ultragenyx Pipeline Improvements.

1.192 "Ultragenyx Pipeline Patents" means all Patents Controlled by Ultragenyx as of the Execution Date and during the Term that: (a) claim the composition of matter of, or the method of making or using an Ultragenyx Pipeline Product; or (b) are otherwise necessary or reasonably useful to Exploit an Ultragenyx Pipeline Product in the Licensed Field. The Ultragenyx Pipeline Patents for the Takeda Territory as of the Execution Date are set forth on Exhibit 1.188.

1.193 "Ultragenyx Pipeline Products" means all products that have entered into Clinical Trials and are Controlled by Ultragenyx or its Affiliates during the Collaboration Term and that Ultragenyx or its Affiliates have rights to Commercialize in the Takeda ROFN Territory, [***]. For purposes of this Section 1.193, "Controlled" shall not include [***]

[***].

1.194 "Ultragenyx Product Infringement" has the meaning set forth in Section 12.6(b)(i).

1.195 "UX[***]" means the compound having Ultragenyx reference number UX[***] as further described on Exhibit 1.195.

1.196 "UX[***]" means the compound having Ultragenyx reference number UX[***] as further described on Exhibit 1.195.

1.197 "UX[***]" means the compound having Ultragenyx reference number UX[***] as further described on Exhibit 1.195.

1.198 "UX[***]" means the compound having Ultragenyx reference number UX[***] as further described on Exhibit 1.195.

1.199 "UX[***]" means the compound having Ultragenyx reference number UX[***] as further described on Exhibit 1.195.

1.200 "Valid Claim" means a claim of an issued and unexpired Patent included within the Takeda Patents, the Ultragenyx Patents or the Joint Patents, to the extent such claim has not been revoked, held invalid or unenforceable by a patent office, court or other governmental agency of competent jurisdiction in a final order, from which no further appeal can be taken, and which claim has not been disclaimed, denied or admitted to be invalid or unenforceable through reissue, re-examination or disclaimer.

1.201 "Validation Research Plan" has the meaning set forth in Section 6.2(b).

ARTICLE 2 – OVERVIEW; MANAGEMENT

2.1 Joint Steering Committee for Licensed Products.

(a) **Formation and Purpose**. Within thirty (30) days after the Effective Date, the Parties shall promptly establish and convene a Joint Steering Committee (the "Joint Steering Committee" or "JSC") in accordance with Section 2.3(c)(i) that will direct and oversee activities relating to the Licensed Products under this Agreement. The JSC shall consist of representatives and operate by the procedures in accordance with Section 2.3. Except as otherwise provided herein, the role of the Joint Steering Committee shall be:

(i) to encourage and facilitate ongoing communication and cooperation between the Parties with respect to the Exploitation by the Parties of Licensed Products in the Licensed Field;

(ii) to serve as a forum for sharing discoveries and exchanging data and results generated by each Party relating to additional compounds Covered by the Licensed [***] Patent;

(iii) to evaluate and approve the inclusion as Licensed Analog Compounds of additional compounds that are Covered by the Licensed [***] Patent but that do not meet the definition of Licensed Analog Compounds [***];

(iv) to evaluate and approve the exclusion from the definition of Licensed Analog Compounds of additional compounds that are Covered by the Licensed [***] Patent [***];

(v) to review and discuss [***] Development Plans and any proposed amendments or revisions to the [***] Development Plans;

(vi) to review and discuss Commercialization Plans including the review and discussion of any amendments to such Commercialization Plans;

(vii) to review and discuss Licensed Product regulatory issues, including those raised by the joint regulatory affairs working group established pursuant to Section 2.1(a)(viii) and Section 9.4(a);

(viii) to establish other such working groups or subcommittees, as needed to further the purposes of the Agreement relating to Licensed Products, as mutually agreed by the Parties in writing;

(ix) to resolve any disputes referred to the JSC; and

(x) to approve or decide such other matters as provided in this Agreement.

(b) **JSC Decisions; Final Decision Authority.**

(i) The JSC will make good faith efforts to make all decisions by consensus. Except as set forth in Section 2.1(b)(ii), actions to be taken by the Joint Steering Committee shall be taken only following unanimous vote, with each Party's representatives collectively having one (1) vote. If the Joint Steering Committee fails to reach unanimous agreement on a matter before it for decision for a period in excess of fifteen (15) days from the date first presented to the JSC in writing, either Party may submit such matter for resolution to the Senior Officers of the Parties for attempted resolution by good faith negotiation within thirty (30) days after such notice is received by the Senior Officers.

(ii) If the Senior Officers of the Parties are unable to resolve such dispute within such thirty (30) day period, such dispute shall be resolved during the Term as follows. For the avoidance of doubt, the right of a Party to make final decisions with respect to any issue

shall not otherwise diminish or eliminate such Party's obligations under this Agreement, including its obligation to exercise Commercially Reasonable Efforts where required herein.

(A) Subject to Sections 2.1(b)(ii)(D) and 2.1(b)(ii)(E) and provided that such decision does not result in an increase in the scope of work or costs associated with the performance of any activities by Takeda under this Agreement, Ultragenyx will have final decision making authority over [***]; and

(B) Takeda will have final decision making authority over [***].

(C) Takeda will have final decision making authority over [***].

(D) If Ultragenyx exercises the [***] Option within the [***] Option Term for the co-Development and co-Commercialization of Licensed [***] Products in the Takeda Field in the Territory, Takeda will have final decision making authority over [***].

(E) If Ultragenyx does not exercise the [***] Option within the [***] Option Term for the co-Development and co-Commercialization of Licensed [***] Products in the Takeda Field in the Territory, (a) Ultragenyx will continue to have final decision making authority over [***], and (b) Takeda will continue to have final decision making authority over [***].

(F) Takeda shall have final decision making authority over [***];

(G) Ultragenyx shall have final decision making authority over [***].

(iii) Neither Party shall have the final decision making authority for any other matter under the purview of the JSC and not covered by subsections (A)-(G), and the status quo shall persist with respect to such matter if the Parties are unable to agree. For clarity, the Parties anticipate that Licensed Option Products and Exercised Products will be governed by separate committees and final decision making authority to be established pursuant to the applicable Option Product License Agreement or Exercised Product License Agreement, respectively.

(c) **Discontinuation of JSC.** Upon [***] or any time thereafter, Ultragenyx shall have the right, upon written notice to Takeda, to

discontinue its participation in the JSC. Once Ultragenyx has provided such notice to Takeda, the JSC shall have no further obligations under this Agreement and, thereafter, Takeda shall have final decision making authority with respect to the topics that were otherwise determined by the JSC, subject to the other terms and conditions of this Agreement.

2.2 **Joint Research Committee for Collaboration Activities**.

(a) **Formation and Purpose**. Within thirty (30) days after the Effective Date, the Parties shall promptly establish and convene a Joint Research Committee (the "Joint Research Committee" or "JRC") in accordance with Section 2.3(c)(i) for the overall coordination and oversight of the Collaboration Activities. The JRC shall consist of representatives and operate by the procedures in accordance with Section 2.3. Except as otherwise provided herein, the Joint Research Committee shall be responsible for supporting the [***] in assessing, prioritizing, and advancing Takeda's rare genetic disease products, including the following specific activities (collectively, "Collaboration Activities"):

(i) review and approve the Validation Research Plan and any amendments thereto;

(ii) review and approve the Option Product Research Plans and any amendments thereto;

(iii) review and approve any amendments to the [***] Research Plan;

(iv) evaluate and prioritize [***];

(v) support the overall direction of Candidate Product and Option Product strategy;

(vi) identify, define, and support collaborations with key experts and investigators and other third parties in support of the prioritized Candidate Products, Option Products and related indications;

(vii) identify and implement opportunities [***];

(viii) determine the [***]; and

(ix) oversee and manage the secondee program provided for in Section 2.6.

(b) **Termination of Responsibilities.** Upon execution of an Option Product License Agreement for an Option Product, the JRC will no longer have any responsibility over or decision making authority relating to such Option Product.

(c) **JRC Decisions; Final Decision Authority**.

(i) The JRC will make good faith efforts to make all decisions by consensus Except as set forth in Section 2.2(c)(ii), actions to be taken by the Joint Research Committee shall be taken only following unanimous vote, with each Party's representatives collectively having one (1) vote. If the Joint Research Committee fails to reach unanimous agreement on a matter before it for decision for a period in excess of fifteen (15) days from the date first presented to the JRC in writing, either Party may submit such matter for resolution to the Senior Officers of the Parties for attempted resolution by good faith negotiation within thirty (30) days after such notice is received among the Senior Officers.

(ii) If the Senior Officers of the Parties are unable to resolve such dispute within such thirty (30) day period, such dispute shall be resolved during the Collaboration Term as follows. For the avoidance of doubt, the right of a Party to make final decisions with respect to any issue shall not otherwise diminish or eliminate such Party's obligations under this Agreement, including its obligation to exercise Commercially Reasonable Efforts where required herein.

(A) Ultragenyx will have final decision making authority over [***];

(B) The Parties must mutually agree on the scope of Research Support to be provided by Takeda. If the Parties are unable to unanimously agree on the scope of the Research Support to be provided, then no Research Support shall be provided;

(C) Takeda will have final decision making authority over [***]; and

(D) Neither Party shall have the final decision making authority for any other matter under the purview of the JRC and not covered by subsections (A)-(C), and the status quo shall persist with respect to such matter if the Parties are unable to agree. For clarity, the Parties anticipate that Licensed Option Products will be governed by a separate committee and final decision making authority to be established pursuant to the Option Product License Agreement.

2.3 **Committee Membership and Procedures**.

(a) **Membership.** Takeda and Ultragenyx shall each designate an equal number of representatives to serve on the JSC and the JRC (each, a "Committee") by written notices to the other Party. Promptly after the Effective Date, each Party shall designate three (3)

representatives for the JSC and three (3) representatives for the JRC. Each Committee may elect to vary the number of representatives from time to time during the Term; provided that each Committee shall maintain an equal number of representatives from each Party. Each representative shall have the appropriate level of experience in the subject area of the Committee, and at least one (1) representative shall have sufficient seniority within the applicable Party's organization to have the necessary decision-making authority in order for the Committee to fulfill its responsibilities. Either Party may designate substitutes for its Committee representatives if one (1) or more of such Party's designated representatives is unable to be present at a meeting. From time to time each Party may replace its Committee representatives by written notice to the other Party specifying the prior representative(s) and their replacement(s).

(b) **Chairperson**. Each Committee will have two chairpersons, one designated by each of the Parties. The chairpersons shall be responsible for calling and convening meetings, but shall have no special authority over the other members of the Committee, and shall have no additional voting rights. The chairpersons (or their designates) shall jointly: (i) prepare and circulate an agenda reasonably in advance of each upcoming meeting; and (ii) prepare and issue minutes of each Committee meeting within thirty (30) days thereafter. Such minutes shall not be finalized until each Committee representative reviews and approves such minutes in writing; provided that any minutes shall be deemed approved unless a member of such Committee objects to the accuracy of such minutes within fifteen (15) days after the circulation of the minutes.

(c) **Meetings**.

(i) **Committee Meetings.** Each Committee shall meet at least once each Calendar Quarter. Additional meetings of the Committees may be held with the consent of each Party (such consent not to be unreasonably withheld, conditioned or delayed), as required under this Agreement. In the case of any dispute referred to a Committee, such meeting shall be held within five (5) Business Days following referral to the Committee, or as soon as reasonably possible.

(ii) **General Requirements.** Meetings of a Committee shall be effective only if a majority of representatives of each Party are present or participating. Other than the initial meeting, which shall be held in person, a Committee may meet either (A) in person at either Party's facilities or at such locations as the Parties may otherwise agree; or (B) by audio or video teleconference. Additional non-members of a Committee having relevant experience may from time to time be invited to participate in a Committee meeting, provided that such participants shall have no voting rights or powers. Non-member participants who are not employees of a Party or its Affiliates shall only be allowed to attend if: (i) the other Party's representatives have consented to the attendance (such consent not to be unreasonably withheld, conditioned or delayed); and (ii) such non-member participant is subject to confidentiality and non-use obligations at least as restrictive as those set forth in this Agreement. Each Party shall be responsible for all of its own expenses incurred in connection with participating in the Committees including all travel and all expenses associated with an initial alliance kick-off meeting. All other expenses incurred by a Committee in furtherance of a meeting, such as expenses associated with off-site meetings, shall be shared equally by the Parties.

2.4 **Alliance Managers**. Promptly following the Effective Date, each Party shall designate in writing an Alliance Manager to serve as the primary point of contact for the Parties regarding all collaboration and transition activities contemplated under this Agreement. Each Alliance Manager shall facilitate communication and coordination of the Parties' activities under this Agreement relating to the Products and shall plan the Committee meetings. The Alliance Managers shall be allowed to attend Committee meetings as non-voting observers.

2.5 **Authority**. The Parties agree that, in voting on matters as described in this ARTICLE 2, it shall be conclusively presumed that unless otherwise explicitly stated, each voting member of a Committee has the authority and approval of such member's respective senior management in casting his or her vote. Each Committee shall have only the powers assigned expressly to it in this ARTICLE 2 and elsewhere in this Agreement, and shall not have any power to amend, modify or waive compliance with this Agreement.

2.6 **Takeda Secondee.** Takeda shall have the right, at its own expense, to place one employee of Takeda or its Affiliates, who is reasonably acceptable to Ultragenyx, as a secondee with Ultragenyx at any time during the Collaboration Term; provided that such secondee shall enter into a confidentiality agreement with Ultragenyx prior to placement. Takeda may, one or more times during the Collaboration Term, substitute such employee with another employee of Takeda or its Affiliates.

ARTICLE 3 – LICENSES FOR [***] AND ANALOGS

3.1 **Licenses from Takeda to Ultragenyx.** Subject to the terms and conditions of this Agreement, Takeda hereby grants to Ultragenyx in the Territory during the Term:

(a) an exclusive (even as to Takeda and its Affiliates, subject to the retention of rights to conduct activities under the [***] Development Plan) license, with the right to grant sublicenses solely in accordance with Section 3.3, under the Licensed [***] Technology, Licensed Product Improvements Controlled by Takeda or its Affiliates, Licensed Product Improvement Patents Controlled by Takeda or its Affiliates, and Joint Intellectual Property to Exploit the Licensed [***] Products in the Ultragenyx Field;

(b) a co-exclusive license, without the right to grant sublicenses, under the Licensed [***] Technology, Licensed Product Improvements Controlled by Takeda or its Affiliates, Licensed Product Improvement Patents Controlled by Takeda or its Affiliates, and Joint Intellectual Property to conduct activities under the [***] Development Plan in the Takeda Field in the Territory; and

(c) an exclusive (even as to Takeda and its Affiliates) license, including the right to grant sublicenses solely in accordance with Section 3.3, under the Licensed [***] Technology, Licensed Product Improvements Controlled by Takeda or its Affiliates, Licensed Product Improvement Patents Controlled by Takeda or its Affiliates, and Joint Intellectual Property to Exploit the Licensed Analog Compounds and Licensed Analog Products in the Licensed Field in the Territory; provided, however, that, notwithstanding the licenses granted in this Section 3.1(c), at any time during the Term Ultragenyx shall not, and shall cause its Affiliates not to (i)

directly or indirectly Exploit any Licensed Analog Product in the Takeda Field or (ii) license, authorize, appoint, or otherwise enable any Third Party to, directly or indirectly, Exploit any Licensed Analog Product in the Takeda Field.

3.2 **Licenses from Ultragenyx to Takeda.** Subject to the terms and conditions of this Agreement, Ultragenyx hereby grants to Takeda in the Territory during the Term:

(a) an exclusive (even as to Ultragenyx and its Affiliates, subject to the retention of rights to conduct activities under the [***] Development Plan) license, with the right to grant sublicenses under multiple tiers solely in accordance with Section 3.3, under the Ultragenyx [***] Technology**,** Licensed Product Improvements Controlled by Ultragenyx or its Affiliates, Licensed Product Improvement Patents Controlled by Ultragenyx or its Affiliates, and Joint Intellectual Property to (i) Exploit the Licensed [***] Products in the Takeda Field in the Territory, and (ii) Exploit any structures Covered by the Licensed [***] Patent, other than with respect to Licensed Analog Compounds, in the Takeda Field in the Territory.

(b) a co-exclusive license, without the right to grant sublicenses, under the Ultragenyx [***] Technology**,** Licensed Product Improvements Controlled by Ultragenyx or its Affiliates, Licensed Product Improvement Patents Controlled by Ultragenyx or its Affiliates, and Joint Intellectual Property to conduct activities under the [***] Development Plan in the Ultragenyx Field in the Territory and to perform the activities under the [***] Development Plan.

3.3 **Sublicensing**. Each Party shall have the right to grant sublicenses, through multiple tiers, of the rights granted to such Party under Sections 3.1(a) and 3.1(c) (in the case of Ultragenyx) and Section 3.2(a) (in the case of Takeda), to its Affiliates and to Third Parties; provided, however that (a) subject to Section 5.2, Ultragenyx shall not grant a sublicense of the rights granted to it under (i) Section 3.1(a) to a Third Party without the prior written consent of Takeda (not to be unreasonably withheld, conditioned or delayed) or (ii) Section 3.1(c) in the Takeda Field and (b) Takeda shall not grant a sublicense of the rights granted to it under Section 3.2(a) to a Third Party without the prior written consent of Ultragenyx (not to be unreasonably withheld, conditioned or delayed). Each sublicense shall refer to and be subordinate to this Agreement and, except to the extent the Parties otherwise agree in writing, any sublicense must be consistent in all material respects with the terms and conditions of this Agreement. Upon termination of this Agreement, any sublicense granted by Ultragenyx to a Third Party shall continue and be transferred to Takeda and any sublicense granted by Takeda to a Third Party shall continue and be transferred to Ultragenyx; provided that such sublicenses comply with the requirements of this Section 3.3. Each Party shall remain responsible for the performance of this Agreement and the performance of its sublicensees hereunder.

3.4 **No Implied Licenses**. No license or other right is or shall be created or granted hereunder by implication, estoppel, or otherwise. All licenses and rights are or shall be granted only as expressly provided in this Agreement. All rights not expressly granted by a Party under this Agreement are reserved by the Party and may not be used by the other Party for any purpose.

ARTICLE 4 – LICENSED PRODUCT DEVELOPMENT

4.1 **Overview of Product Development**. The Parties desire and intend to collaborate with respect to the Development of the Licensed Product in the Licensed Field in the Territory, to the extent set forth in this Agreement. Takeda's Development of the Licensed [***] Products in the Takeda Field and Ultragenyx's Development of the Licensed [***] Products in the Ultragenyx Field and Licensed Analog Products in the Licensed Field shall be conducted in a manner consistent with the [***] Development Plans and using Commercially Reasonable Efforts.

4.2 **Transition and Exchange of Know-How**

(a) **Transition from Takeda to Ultragenyx.** As soon as practicable after the Effective Date, the Parties will cooperate and act in good faith to support the transition of the Licensed [***] Product from Takeda to Ultragenyx in the Ultragenyx Field and, solely for purposes of Ultragenyx's performance of its obligations under Section 4.3(a)(ii), in the Takeda Field, at no additional consideration payable to Takeda, including the (i) transition and, to the extent appropriate, assignment of Regulatory Materials and Regulatory Approvals covering the Licensed [***] Product in the Ultragenyx Field and, solely for purposes of Ultragenyx's performance of its obligations under Section 4.3(a)(ii), in the Takeda Field, from Takeda to Ultragenyx, (ii) sharing of the Licensed [***] Know-How with Ultragenyx to the extent necessary or reasonably useful for the use of the Licensed [***] Product and the Licensed Analog Products for and implementation of the Initial [***] Development Plan, and (iii) transferring to Ultragenyx, at no cost to Ultragenyx, those biological materials or chemical compounds related to the Licensed [***] Product Controlled by Takeda as of the Execution Date as are necessary for Ultragenyx to perform the activities allocated to it under the Initial [***] Development Plan. Takeda will also use Commercially Reasonable Efforts, at Ultragenyx's sole cost and expense, to assign or sublicense to Ultragenyx any existing Third Party agreements that are necessary or reasonably useful for the Exploitation of a Licensed [***] Product in the Ultragenyx Field in the Territory. Within forty-five (45) days after the receipt of an invoice from Takeda reflecting the costs and expenses of such assignment or sublicense, Ultragenyx shall pay the invoiced amounts to Takeda.

(b) **Know-How Sharing by Ultragenyx.** Ultragenyx shall provide to Takeda, promptly after the Effective Date and during the Term upon Ultragenyx Know-How being obtained or generated by Ultragenyx, at no additional cost or expense to Takeda, all such Ultragenyx Know-How as is necessary or reasonably useful to enable Takeda: (a) to perform its obligations under this Agreement; (b) to Exploit the Licensed [***] Product in the Takeda Field, and (c) to Exploit any structures Covered by the Licensed [***] Patent, other than with respect to Licensed Analog Compounds, in the Takeda Field in the Territory.

4.3 **Development Activities**.

(a) Throughout the Term, Ultragenyx will use Commercially Reasonable Efforts to (i) Exploit a Licensed [***] Product or Licensed Analog Product in the Ultragenyx Field in the Territory and (ii) complete Development activities for a Licensed [***] Product in the Takeda

Field, in each case at Ultragenyx's sole expense and pursuant to the Initial [***] Development Plan.

(b) If the Parties mutually agree to conduct other Development activities with respect to a Licensed [***] Product other than as set forth in the Initial [***] Development Plan, then the Parties shall prepare a plan (including timeline and budget) covering the Development activities to be completed, the Party responsible for completing such activities, and the Party responsible for the associated costs (together with the Initial [***] Development Plan, the "[***] Development Plans").

(c) If Ultragenyx elects to pursue Development of a Licensed Analog Product, Ultragenyx will use Commercially Reasonable Efforts to Exploit such Licensed Analog Product in the Ultragenyx Field in the Territory at Ultragenyx's sole expense and pursuant to a [***] Development Plan for such Licensed Analog Product.

(d) At Ultragenyx's sole expense, Takeda, using Commercially Reasonable Efforts, will (i) conduct initial manufacturing process development and scale-up activities for the Licensed Products as set forth in the Initial [***] Development Plan and in accordance with the agreed upon budget contained therein, (ii) will work with Ultragenyx to transfer Licensed [***] Know-How as necessary or reasonably useful for Development and for the purposes of completing Regulatory Applications, initiating Clinical Trials and for transitioning manufacturing activities to Ultragenyx, and (iii) conduct such other Development and Manufacturing activities as may be mutually agreed by the Parties.

(e) Each Party shall conduct its activities under this Agreement in good scientific manner and in compliance in all material respects with all Applicable Laws, including, GCP, GLP, and GMP.

(f) If Ultragenyx breaches its obligations under Section 4.3(a) or 4.3(c) or is otherwise no longer actively conducting Development of a Licensed [***] Compound and Licensed [***] Product in any indication in the Ultragenyx Field, then [***] of the date Ultragenyx stopped actively conducting such Development, the Ultragenyx [***] License for the Licensed [***] Compound and Licensed [***] Product shall terminate and, [***] of such event, such license shall revert to Takeda and the terms of Section 15.7(c) shall apply with respect to such Compound and Product; provided, that, upon the reversion of rights to Takeda, Takeda shall not develop such Product in the Ultragenyx Field except in accordance with Takeda's exercise of the Takeda Option or right of first negotiation pursuant to ARTICLE 8. If, prior to the effective date of such reversion, Ultragenyx determines it wishes to license such Compound or Product from Takeda in the Ultragenyx Field, Ultragenyx may provide written notice to Takeda. Following receipt of such notice, Takeda and Ultragenyx will negotiate in good faith such license agreement for a period of [***] thereafter, which period may be extended by mutual agreement. Any resulting license agreement will be subject to Takeda's exercise of the Takeda Option or right of first negotiation pursuant to ARTICLE 8.

(g) Neither Party may Develop Licensed [***] Products in the Ultragenyx Field except as set forth in the [***] Development Plan. Takeda shall have the sole discretion to Develop Licensed [***] Products in the Takeda Field.

4.4 **Clinical Trial Registry**.

(a) Ultragenyx shall be responsible for registering any Clinical Trial performed pursuant to the [***] Development Plans in the appropriate clinical trial registry (e.g., clinicaltrials.gov) and posting the results of such Clinical Trials as required by Applicable Laws.

(b) The posting of any results to a clinical trial registry in accordance with this Section 4.4 shall be considered a "publication" and subject to the Parties' obligations set forth in Section 14.9.

4.5 **Records; Disclosure of Data and Results.** In conformity with standard pharmaceutical industry practices and the terms and conditions of this Agreement, each Party shall prepare and maintain, or shall cause to be prepared and maintained, complete and accurate written records, accounts, notes, reports and data with respect to activities conducted pursuant to the [***] Development Plans for a minimum of three (3) years following the end of the Calendar Year to which they pertain (or such longer period as may be required by Applicable Laws) and, upon the other Party's reasonable written request, shall send legible copies (in English and in electronic format) of the aforesaid to the other Party, to the extent not already provided, throughout the Term and for a minimum of twelve (12) months following the Term. Upon reasonable advance notice, at the request of the JSC, each Party agrees to make its employees and consultants reasonably available at their respective places of employment to consult with the other Party on issues arising in connection with the [***] Development Plans. In accordance with the reporting format and schedule approved by the JSC, each Party shall promptly and fully disclose to the other Party in writing all data, including preclinical data, Clinical Trial data, formulation data and manufacturing data, generated by or on behalf of such Party with respect to the Products in the Licensed Field. Without limiting the foregoing: (a) Ultragenyx shall keep Takeda regularly and fully informed by reporting to the JSC on a quarterly basis regarding the Development of Licensed Products in the Ultragenyx Field in the Territory by Ultragenyx, its Affiliates and sublicensees, including information regarding the status of Clinical Trials, filing of Regulatory Materials and receipt of Regulatory Approval with respect to the Products in the Ultragenyx Field in the Territory; (b) on at least an annual basis (but in any event, no later than December 1 of each Calendar Year), each Party, as applicable, shall submit to the JSC proposed updates and amendments, as appropriate, to the [***] Development Plans; and (c) Takeda shall keep Ultragenyx regularly informed by reporting to the JSC on a quarterly basis regarding the Development of Licensed Products in the Takeda Field by Takeda, its Affiliates and sublicensees, including information regarding the status of any Clinical Trials, filing of Regulatory Materials and receipt of Regulatory Approval with respect to the Products in the Takeda Field in the Territory.

ARTICLE 5– [***] CO-DEVELOPMENT AND CO-COMMERCIALIZATION

5.1 **Co-Development and Co-Commercialization Negotiation for Takeda Field**.

(a) As soon as practicable, but no later than [***], Ultragenyx shall deliver to Takeda the Final [***] Data Package for such Licensed Product. For a period of [***] following the deadline for delivery of such Final [***] Data Package for the first Licensed [***] Product or Takeda's earlier receipt of such Final [***] Data Package (the "[***] Option Term"), Ultragenyx will have the right to exercise an exclusive option to co-Develop and co-Commercialize the Licensed [***] Products in the Takeda Field in the Territory (the "[***] Option"). Upon exercise of the [***] Option prior to the expiration of the [***] Option Term, the Parties will negotiate in good faith, for a period of up to [***] (the "[***] License Negotiation Period"), the terms relating to the co-Development and co-Commercialization of the Licensed [***] Products in the Takeda Field in the Territory (other than the rights regarding final decision making authority of the Parties, which will be as set forth in Section 2.1(b)(ii)(D)).

(b) If Ultragenyx exercises the [***] Option within the [***] Option Term and the Parties reach agreement regarding the co-Development and co-Commercialization of the Licensed [***] Product in the Takeda Field within the [***] License Negotiation Period, such agreement, including any needed modification to the Ultragenyx [***] License and Takeda [***] License, will be entered into by the Parties or their designated Affiliates. Such agreement shall provide that, if Ultragenyx terminates the Development of Licensed [***] Products in the Ultragenyx Field, then Ultragenyx shall have the right to terminate such co-Development and co- Commercialization of Licensed [***] Products in the Takeda Field upon providing Takeda with the following prior written notice: (i) if the Licensed [***] Product is in Development at the time of termination, [***], and (ii) if the Licensed [***] Product is being Commercialized at the time of termination, [***].

(c) If Ultragenyx exercises the [***] Option within the [***] Option Term and the Parties fail to reach an agreement regarding the co-Development and co-Commercialization of the Licensed [***] Product in the Takeda Field within the [***] License Negotiation Period, then Takeda and Ultragenyx shall have the right to submit their proposed terms for such co- Development and co-Commercialization of the Licensed [***] Products in the Takeda Field in the Territory to binding arbitration as set forth in Section 16.3; provided, however, that the rights regarding the final decision making authority of the Parties as set forth in Section 2.1(b)(ii)(D) will not be subject to modification in such arbitration.

5.2 **Takeda Right of First Negotiation for the Ultragenyx Field.** Notwithstanding Ultragenyx's right to sublicense under Section 3.3, Ultragenyx does not have the right to enter into an agreement with any Third Party for the co-Development and/or co-Commercialization (including co-promotion) of the Licensed Product in the Ultragenyx Field except in accordance with the terms of this Section 5.2. If Ultragenyx intends to co-Develop and/or co-Commercialize (including co-promote) with a Third Party a Licensed Product in the Ultragenyx Field, Ultragenyx will provide Takeda with prior written notice of such intent and, for a period of [***] after receipt of such notice, Takeda will have a right of first negotiation to enter into a definitive agreement with Ultragenyx for such co-Development and/or co-Commercialization (including co-promotion). If the Parties fail to enter into a definitive

agreement prior to the expiration of [***], Ultragenyx will have the right to enter into a definitive agreement with a Third Party (including via sublicensing as set forth in Section 3.3) for the co-Development and/or co-Commercialization (including co- promotion) of the Licensed Product in the Ultragenyx Field; provided, that, [***], Ultragenyx shall not enter into such a definitive agreement with a Third Party on terms, when viewed as a whole, that are less favorable to Ultragenyx than the terms last offered to Ultragenyx by Takeda.

5.3 **Commercialization Plans.** Each Party shall submit a Commercialization Plan to the JSC for discussion no less [***] prior to the anticipated date of such Party obtaining Regulatory Approval for a Licensed Product. Thereafter, each Party shall provide a copy of the then-current Commercialization Plan to the JSC at least once each Calendar Year during the Licensed Product Royalty Term and Takeda Royalty Term, as applicable.

5.4 **Commercialization Activities.**

(a) **Ultragenyx Commercialization**. Ultragenyx shall use Commercially Reasonable Efforts to Commercialize the Licensed Product in the Ultragenyx Field in the Territory throughout the Term. Subject to any modifications based on agreements reached pursuant to Sections 5.1 and 5.2, Ultragenyx's Commercially Reasonable Efforts requirements and the provisions of Section 2.1(b), Ultragenyx has sole discretion relating to all aspects of the Commercialization of Licensed Products in the Ultragenyx Field in the Territory. As between the Parties, Ultragenyx shall bear all of the costs and expenses incurred in connection with all such Commercialization activities. On an annual basis, and no later than March 1 of each Calendar Year following the First Commercial Sale of a Licensed Product in the Ultragenyx Field in the Territory, Ultragenyx shall present a reasonably detailed written report to the JSC summarizing Ultragenyx's overall Commercialization activities undertaken during the previous Calendar Year with respect to the Licensed Products in the Ultragenyx Field.

(b) **Takeda Commercialization**. Subject to any modifications based on agreements reached pursuant to Sections 5.1 and 5.2 and the provisions of Section 2.1(b), Takeda has sole discretion relating to the Commercialization of Licensed [***] Products in the Takeda Field in the Territory. As between the Parties, Takeda shall bear all of the costs and expenses incurred in connection with all such Commercialization activities.

5.5 **Trademarks**.

(a) **Ownership.** Each Party shall own, throughout the world, each Product trademark that it develops for a Product in its Field in the Territory (each a "Product Trademark"). All goodwill attributable to a Party's Product Trademark generated by the Commercialization of a Product bearing such mark shall inure to the benefit of such Party.

(b) **Use.** Neither Party shall be obligated to use the other Party's Product Trademark or House Marks except to the extent required by Applicable Law or regulatory requirement. Neither Party shall, during the Term or thereafter, adopt, register or use any trademark, trade

name, brand name, symbol or logo that is identical, or confusingly similar, to the other Party's Product Trademarks.

(c) **Filing; Maintenance.** Each Party shall solely be responsible for, and shall solely bear all costs associated with maintenance and enforcement of, such Party's Product Trademark.

ARTICLE 6 – RESEARCH COLLABORATION

6.1 **Research Collaboration Generally**. The Parties will conduct research of Takeda's [***] Compound and Candidate Products as set forth in this Agreement. As further described below, the Candidate Products will be selected from the Takeda-Controlled compounds listed on Exhibit 6.1 attached hereto, as may be amended from time to time by Takeda in its sole discretion (the "Listed Compounds").

6.2 **Nomination of Candidate Products and Validation Research**.

(a) **Nomination**. Either Party may nominate compounds from the Listed Compounds for consideration and approval by the JRC as candidate products under this Agreement (upon such approval, each such Listed Compound shall thereafter be a "Candidate Product"). The JRC may select up to five (5) Candidate Products for validation pursuant to Section 6.2(b) at any one time. If five (5) Candidate Products have been selected at any one time, neither Party may nominate any additional Listed Compound to be considered as a Candidate Product unless and until the Parties determine, after the completion or termination of research activities under the applicable Validation Research Plan, that a Candidate Product will not be nominated as an Option Product.

(b) **Validation Research Plan**. Takeda will design, with input from Ultragenyx, a research plan and budget for the initial validation for each Candidate Product (each, a "Validation Research Plan"), with each such Validation Research Plan intended to sufficiently include the activities required to provide information and data necessary for the JRC to determine whether to nominate a Candidate Product as an Option Product. Each Validation Research Plan will be submitted to the JRC for approval (for which Takeda will have final decision-making authority in accordance with Section 2(c)(ii)(C)) and will be funded by Takeda and performed by or on behalf of Takeda, in Takeda's sole discretion.

6.3 **[***] Research Plan and Transition**

(a) During the Collaboration Term with respect to the [***] Products, the Parties will use Commercially Reasonable Efforts to Exploit the [***] Products, at Ultragenyx's sole expense, pursuant to the initial research plan and budget for the [***] Products attached hereto as Exhibit 6.3(a) (the "[***] Research Plan"). Pursuant to the [***] Research Plan and in accordance with the associated budget, at Ultragenyx's sole expense, Takeda will use Commercially Reasonable Efforts to conduct initial Manufacturing process development and scale-up of the [***] Products, as agreed by the Parties. For clarity, there will not be any Validation Research Plan for the [***] Products.

(b) During the Collaboration Term with respect to the [***] Products, the Parties shall cooperate and act in good faith to support the transition of the [***] Products from Takeda to Ultragenyx in the Licensed Field to the extent necessary or reasonably useful for Ultragenyx to perform the [***] Research Plan, including the transition of Option Product Know-How with respect to the [***] Products. [***].

6.4 **Option Product Research Plan**. During the Collaboration Term with respect to each Option Product for which there is an agreed Option Product Research Plan, Ultragenyx will use Commercially Reasonable Efforts to Exploit each Option Product in accordance with the applicable Option Product Research Plan.

6.5 **Limited Licenses During the Collaboration Term**.

(a) **License to Ultragenyx**.

(i) Upon selection of a Candidate Product as an Option Product by the JRC and as of the Effective Date with respect to [***] Products, Takeda hereby grants to Ultragenyx a limited, co-exclusive (with Takeda and its Affiliates), non-transferable, non-sublicensable, royalty-free license under the Option Product Technology, Option Product Improvements Controlled by Takeda or its Affiliates, Option Product Improvement Patents Controlled by Takeda or its Affiliates, and Joint Intellectual Property to Exploit the Option Product solely in accordance with the activities to be performed by Ultragenyx under the Option Product Research Plan.

(ii) The foregoing license under Section 6.5(a)(i) will continue on an Option Product-by-Option Product basis until the earlier of (A) execution of an Option Product License Agreement, (B) failure by the Parties to enter into an Option Product License Agreement by the expiration of the applicable Option Negotiation Period, or (C) expiration or termination of the Collaboration Term, at which time such Option Product shall be a Terminated Product and all rights to such Option Product will revert to Takeda in accordance with Section 15.7(c); provided that, if in the case of (C), an Option Negotiation Period is then ongoing, the Collaboration Term with respect to such Option Product will automatically extend until the earlier of (1) expiration of such Option Negotiation Period or (2) execution of the applicable Option Product License Agreement.

(b) **License to Takeda**. During the Collaboration Term, with respect to each Research Product, Ultragenyx hereby grants to Takeda a limited, non-exclusive, non- transferable, non-sublicensable, royalty-free license, under all Ultragenyx Intellectual Property, Option Product Improvements Controlled by Ultragenyx and Joint Intellectual Property for use in the Licensed Field in the Territory solely to perform its obligations under each Research Plan and to the extent necessary or reasonably useful for Takeda to evaluate a Candidate Product.

(c) **No Implied Licenses**. No license or other right is or shall be created or granted hereunder during the Collaboration Term with respect to any Research Product by implication,

estoppel, or otherwise. All rights not expressly granted by a Party under this Agreement are reserved by such Party and may not be used by the other Party for any purpose.

6.6 **Research Materials Transfer**.

(a) In order to facilitate the activities contemplated by this Agreement, Takeda shall transfer to Ultragenyx, at no cost to Ultragenyx (i) those quantities of [***] Compound Controlled by Takeda as of the Execution Date as are necessary for Ultragenyx to perform the activities allocated to it under the [***] Research Plan and (ii) reasonable quantities of biological materials or chemical compounds Controlled by Takeda at the time a Candidate Product becomes an Option Product for Development of such Option Product (collectively, the "Research Materials") by Ultragenyx in furtherance of the applicable Research Plans. Such transfer shall be pursuant to a mutually agreed upon Research Materials transfer plan and schedule (including, as necessary, a separate agreement with respect to such transfer which the Parties shall enter as soon as practicable (A) after the Effective Date in the case of the foregoing clause (i) or (B) after a Candidate Product becomes an Option Product in the case of the foregoing clause (ii)). Except as otherwise provided for under this Agreement, all such Research Materials will remain the sole property of Takeda, will be used only in furtherance of the activities conducted in accordance with the applicable Research Plans, will not be used or delivered to or for the benefit of any Third Party (except for subcontractors in furtherance of the Research Plans), without the prior written consent of Takeda, and will be used in compliance with Applicable Law. The Research Materials supplied under this Agreement must be used with prudence and appropriate caution in any experimental work because not all of their characteristics may be known. Takeda will provide Ultragenyx the most current material safety data sheet for the Research Materials upon transfer of any Research Materials.

(b) Except as expressly set forth in this Agreement, THE RESEARCH MATERIALS ARE PROVIDED "AS IS" AND WITHOUT ANY REPRESENTATION OR WARRANTY, EXPRESS OR IMPLIED, INCLUDING ANY IMPLIED WARRANTY OF MERCHANTABILITY OR OF FITNESS FOR ANY PARTICULAR PURPOSE OR ANY WARRANTY THAT THE USE OF THE RESEARCH MATERIALS WILL NOT INFRINGE OR VIOLATE ANY PATENT OR OTHER PROPRIETARY RIGHTS OF ANY THIRD PARTY.

6.7 **General Terms Applicable to Research Plans and Research Activities**.

(a) **Annual Review of Research Plans**. On an annual basis, the Parties, through the JRC, shall review, and as necessary, update and amend the then-current Research Plans, provided that either Party may at any time between annual updates recommend updates or amendments of the then-current plans and associated budget for consideration by the JRC.

(b) **Performance Obligations**. With respect to each Research Plan, Ultragenyx and Takeda shall each use Commercially Reasonable Efforts to execute and perform the activities assigned to it and cooperate with the other Party in the performance of such activities. Each Party shall conduct the activities assigned to it under the Research Plan in a good scientific manner and in compliance in all material respects with Applicable Law, including applicable

national and international (e.g., ICH, GCP, GLP, and GMP) guidelines. If a Research Plan provides for Clinical Trials, the sponsor of such trial shall register and post the results of such trial.

(c) **Records; Disclosure of Data and Results**. Each Party shall prepare and maintain, or shall cause to be prepared and maintained, complete and accurate written records, accounts, notes, reports and data with respect to its activities conducted pursuant to a Research Plan in conformity with Applicable Law and standard pharmaceutical industry practices; provided that in no case shall such records be maintained for less than three (3) years following the Calendar Year to which such records pertain (or such longer period as may be required by Applicable Laws). Upon the other Party's written request, the Party receiving such written request shall send legible copies of the aforesaid to the other Party throughout the Term with respect to such Research Product and for a minimum of twelve (12) months following such Term. Upon reasonable advance notice, at the request of the JRC, each Party agrees to make its employees and consultants reasonably available at their respective places of employment to consult with the other Party on issues arising in connection with each Research Plan. In accordance with the reporting format and schedule approved by the JRC, each Party shall promptly disclose to the other Party in writing all data, including preclinical data, clinical trial data (if any), formulation data and Manufacturing data, generated by or on behalf of such Party with respect to a Research Product in the Licensed Field in the Territory.

(d) **Termination of Research Plan**. In the event the activities under a Research Plan are terminated for any reason, all research thereunder shall cease and the applicable Option Product or [***] Product will be deemed to be a Terminated Product. All Terminated Products shall revert to Takeda pursuant to Section 15.7(c). For clarity, such termination shall not terminate the Collaboration Term for any other purpose under this Agreement.

6.8 **Research Program Expenses.**

(a) **Nomination Evaluation**. Each Party shall be responsible for its own FTEs and any Third Party expenses, in each case, incurred with respect to the nomination, evaluation and selection of Candidate Products in accordance with Section 6.2(a).

(b) **[***] Research Plan**. Ultragenyx shall reimburse Takeda for Takeda's FTE Costs and out-of-pocket Third Party expenses, in each case, incurred by Takeda in furtherance of the completion of those activities assigned to it under the [***] Research Plan and in accordance with the applicable budget, subject to a maximum reimbursement obligation of [***] of such budget or such greater amount as Ultragenyx may approve in advance.

(c) **Validation Research Plan**. Takeda shall be responsible for its own FTEs and any Third Party expenses incurred by Takeda with respect to a Validation Research Plan.

(d) **Option Product Research Plan.** Ultragenyx shall reimburse Takeda for Takeda's FTE Costs and out-of-pocket Third Party expenses, in each case, incurred by Takeda in furtherance of the completion of those activities assigned to it under an Option Product Research Plan and in accordance with the applicable budget, subject to a maximum reimbursement

obligation of [***] of such budget or such greater amount as Ultragenyx may approve in advance.

6.9 **Invoices**. Within forty-five (45) days after the end of each Calendar Quarter, Takeda will provide a written report and invoice to Ultragenyx setting forth in reasonable detail its FTEs and its Third Party expenses recorded in furtherance the [***] Research Plan and Option Product Research Plans. Within sixty (60) days after the receipt of such invoice, Ultragenyx shall pay the undisputed portion of any such invoice. For clarity, making such a payment does not preempt Ultragenyx's audit rights under Section 11.12, which remain in full force and effect. If Ultragenyx in good faith identifies items in an invoice which are disputed, Ultragenyx will notify Takeda in writing, noting its objection to the disputed item(s) with specificity, within ten (10) business days of receipt of the invoice. Takeda will respond to such written notification within ten (10) days of receipt of the disputed notification. Thereafter, the Parties shall negotiate in good faith to resolve the dispute with either Takeda supplying Ultragenyx documentation justifying the charge or reducing or deleting the disputed amount. Any dispute over invoiced amounts due that cannot be resolved by direct good faith negotiation between the Parties shall be resolved in accordance with ARTICLE 16 (Dispute Resolution) of this Agreement; provided further, if the Dispute is not resolved pursuant to Section 16.2, the Parties agree that such Dispute shall be resolved pursuant to Section 16.3.

6.10 **Option Products.**

(a) At any time during the Collaboration Term after the completion of research activities under a Validation Research Plan, either Ultragenyx or Takeda may, through the JRC, nominate a Candidate Product for selection as an Option Product, and the JRC will promptly consider such request. In order for a Candidate Product to become an Option Product, the JRC must agree (by mutual agreement of the Parties' representatives on the JRC) to (i) the selection of the Candidate Product as an Option Product, (ii) a research plan, and budget that identifies the research and development activities which shall be performed and paid for entirely by Ultragenyx (each, an "Option Product Research Plan"), and (iii) key terms, including the territory, field of use, development and commercial responsibilities and financial terms (the "Option Product Key Terms") to serve as the basis for an Option Product License Agreement. For clarity, the Option Product Research Plan for [***] Products is the [***] Research Plan.

(b) The [***] Products are designated as Option Products as of the Effective Date. The Option Product Key Terms for [***] Products are attached hereto as Exhibit 6.10(b).

6.11 **The Ultragenyx Option.** Takeda hereby grants to Ultragenyx, during the applicable Collaboration Term, the exclusive option to obtain, on a product-by-product basis, an exclusive license, with the right to grant sublicenses through multiple tiers, under the Option Product Technology and Joint Intellectual Property to Exploit (a) the [***] Products and (b) up to five (5) other Option Products in the Licensed Field in the Territory (the "Ultragenyx Option"), subject to the terms and conditions set forth in this Agreement including ARTICLE 8.

6.12 **Exercising the Option**.

(a) At any time during the Collaboration Term, Ultragenyx may exercise the Ultragenyx Option regarding an Option Product by notifying Takeda in writing of its intent to exercise the Option with respect to a specific Option Product and negotiate the terms of a license agreement (the "Option Notice"). During the period of time beginning on the effective date of each such Option Notice and ending [***] thereafter, which period may be extended by mutual agreement (the "Option Negotiation Period"), the Parties will conduct good faith negotiations with the intent to agree upon license terms and conclude a definitive license agreement (the "Option Product License Agreement") in accordance with the applicable Option Product Key Terms and other terms that reflect the expected commercial opportunity and development stage of the Option Product. Any such Option Product License Agreement will include provisions to address approvals of any Governmental Authority which are required before effectiveness of such Option Product License Agreement.

(b) If the Parties cannot conclude an Option Product License Agreement during the Option Negotiation Period, Takeda and Ultragenyx shall each have the right to submit the Option Product Key Terms and other terms for a final decision regarding the terms of the Option Product License Agreement pursuant to binding arbitration under Section 16.3. All rights to any Option Product for which the Parties do not enter into an Option Product License Agreement shall revert to Takeda and such Option Product shall be deemed a Terminated Product subject to Section 15.7(c).

ARTICLE 7 – TAKEDA RESEARCH SUPPORT

7.1 **Research Support.** During the Collaboration Term and upon mutual agreement of the Parties, Takeda may provide research support as set forth in this Section 7.1 ("Research Support") to Ultragenyx, at Ultragenyx's sole cost. Such Research Support shall be related to the development of Ultragenyx Pipeline Products (in each case, other than Exercised Products) or Licensed Option Products (in each case, in connection with an Option Product License Agreement), and shall include medicinal chemistry, testing of compounds in disease animal models, drug formulation and clinical development support. If Ultragenyx and Takeda agree that Takeda should provide such Research Support, the confidentiality obligations, access to premises, and other details related to Takeda personnel providing such Research Support to Ultragenyx shall be addressed in a separate agreement between the Parties and such personnel.

7.2 **Expenses and Invoices.** Ultragenyx shall reimburse Takeda for Takeda's FTE Costs and out-of-pocket Third Party expenses, in each case, incurred by Takeda for the provision of the Research Support and in accordance with the applicable budget, subject to a maximum reimbursement obligation of [***] of such budget or such greater amount as Ultragenyx may approve in advance. Within forty-five (45) days after the end of each Calendar Quarter, Takeda will provide a written report and invoice to Ultragenyx setting forth in reasonable detail its FTEs and its Third Party expenses recorded for the Research Support. Within sixty (60) days after the receipt of such invoice, Ultragenyx shall pay the undisputed portion of any such invoice. For clarity, making such a payment does not preempt Ultragenyx's audit rights under Section 11.12, which remain in full force and effect. If Ultragenyx in good faith identifies items in an invoice which are disputed, Ultragenyx will notify Takeda in writing,

noting its objection to the disputed item(s) with specificity, within ten (10) business days of receipt of the invoice. Takeda will respond to such written notification within ten (10) days of receipt of the disputed notification. Thereafter, the Parties shall negotiate in good faith to resolve the dispute with either Takeda supplying Ultragenyx documentation justifying the charge or reducing or deleting the disputed amount. Any dispute over invoiced amounts due that cannot be resolved by direct good faith negotiation between the Parties shall be resolved in accordance with ARTICLE 16 (Dispute Resolution) of this Agreement; provided further, if the Dispute is not resolved pursuant to Section 16.2, the Parties agree that such dispute shall be resolved pursuant to Section 16.3.

7.3 **Patent Ownership.** If Research Support is provided pursuant to Section 7.1 related to an Ultragenyx Pipeline Product (other than an Exercised Product), then, notwithstanding Section
12.1 or any other separate written agreement between the Parties with respect to such Research Support, as between the Parties and regardless of inventorship, Ultragenyx shall own all right, title and interest in and to any Patents related to such Ultragenyx Pipeline Product (other than an Exercised Product in the Exercised Countries) that arise out of such Research Support. For purposes of clarity, following the execution of an Option Product License Agreement or Exercised Product License Agreement, the terms of such license agreement shall govern the handling of activities of the type covered by the definition of Research Support related to the Product(s) that are the subject of the applicable license agreement.

ARTICLE 8 – TAKEDA'S LICENSE OPTION

8.1 **The License Option.** In partial consideration for the premium paid by Takeda to Ultragenyx under the Common Stock Purchase Agreement, Ultragenyx hereby grants to Takeda during the applicable Takeda Option Term, the exclusive option to obtain (the "Takeda Option"), on a product-by-product and country-by-country basis, an exclusive license (even as to Ultragenyx and its Affiliates) to (a) any or all of the Licensed Products in the Ultragenyx Field,
(b) any or all Licensed Option Products in the Licensed Field, and (c) one (1) Ultragenyx Pipeline Product in the Licensed Field, in each case in any or all of the countries in the Takeda Territory. For clarity, if Takeda elects not to exercise the Takeda Option with respect to (i) any Licensed [***] Product, Licensed Analog Product, Licensed Option Product, or Ultragenyx Pipeline Product, or (ii) any country in the Takeda Territory, as the case may be, prior to the expiration of the Takeda Option Term with respect to such Product and/or such country, as applicable, then Takeda shall no longer have any rights under the Takeda Option with respect to such Product and/or such country, as applicable.

8.2 **Exercising the License Option**.

(a) **Preparation and Delivery of the Data Packages**. Ultragenyx shall prepare and deliver to Takeda as soon as reasonably practicable after completion of the applicable Clinical Trials (a) the Final Phase II Data Package for each Licensed [***] Product, Licensed Analog Product, Licensed Option Product and Ultragenyx Pipeline Product (other than [***]) and (b) the Final Phase III Data Package for [***].

(b) **Takeda Review of Research Data Package**. Following Takeda's receipt of the applicable Data Package pursuant to Section 8.2(a) and during the applicable Takeda Option Term, Takeda may review and assess the Data Package to determine whether it will submit the Takeda Option Notice. During this review period, upon Takeda's reasonable request, Ultragenyx shall promptly make available to Takeda: (i) its employees, consultants and independent contractors (subject to the availability of any independent contractors) who performed the activities on behalf of Ultragenyx, including the preparation of the Data Package; and (ii) any additional Information under Ultragenyx's possession and Control related to the applicable products that is reasonably useful in evaluating the Data Package.

(c) **Takeda Option Exercise Mechanics**. Takeda may exercise the Takeda Option for one or more Licensed [***] Products, one or more Licensed Analog Products, one or more Licensed Option Products, and one Ultragenyx Pipeline Product on a country-by-country basis in the Takeda Territory at any time during the applicable Takeda Option Term by providing written notice to Ultragenyx (the "Takeda Option Notice") identifying the applicable Products ("Exercised Products") and countries ("Exercised Countries"); provided, however, that Takeda may exercise the Takeda Option with respect to each Licensed Product only once (i.e., if the Takeda Option is exercised with respect to a particular Licensed Product for fewer than all applicable countries, then additional countries may not be added by additional exercises of the Takeda Option with respect to that particular Licensed Product).

(d) During the period of time beginning on the effective date of the Takeda Option Notice and ending [***], which period may be extended by mutual agreement (the "Takeda Option Negotiation Period"), the Parties will conduct good faith negotiations to conclude a definitive license agreement (the "Exercised Product License Agreement"). Such Exercised Product License Agreement shall include the following:

(i) the following license grant with respect to the Exercised Products in the Exercised Countries, which, to the extent of any conflict, shall supersede the Ultragenyx [***] License and Takeda [***] License and the terms of any Option Product License Agreement: Ultragenyx hereby grants to Takeda an exclusive license (even as to Ultragenyx and its Affiliates), with the right to grant sublicenses through multiple tiers, under the Ultragenyx Intellectual Property and Joint Intellectual Property, to Exploit the Exercised Products in the Ultragenyx Field (where such Exercised Product is a Licensed Product) or the Licensed Field (where such Exercised Product is a Licensed Option Product or Ultragenyx Pipeline Product) in the Exercised Countries;

(ii) financial terms in ARTICLE 11 (and related definitions) applicable to Exercised Products (and no other consideration payable by Takeda);

(iii) provisions to address approvals of any Governmental Authority which are required before effectiveness of the Exercised Product License Agreement;

(iv) provisions to address the prosecution, enforcement and defense of Patents that cover Exercised Products similar to those contained in ARTICLE 12;

(v) the right for Takeda to terminate for convenience upon [***] written notice;

(vi) the right for Takeda to, in lieu of termination for Ultragenyx's material breach or insolvency, receive rights on the basis set forth in Section 15.7(a)(ii)(B);

(vii) provisions that upon the expiration of the Takeda Royalty Term for each Exercised Product in each Exercised Country, Takeda shall have a non-exclusive, fully-paid up and irrevocable license under the Ultragenyx Intellectual Property with respect to such Exercised Product in such Exercised Country in the Ultragenyx Field (for Exercised Products that are Licensed Products) and in the Licensed Field (for Exercised Products that are Option Products or Ultragenyx Products); and ARTICLE 18.

(viii) to the extent applicable, Miscellaneous provisions as contained in

(e) If the Parties cannot conclude the Exercised Product License Agreement during the Takeda Option Negotiation Period, Takeda and Ultragenyx shall each have the right to submit the terms for a final decision regarding the terms (other than those specified in Section 8.2(d)) of the Exercised Product License Agreement pursuant to binding arbitration under Section 16.3. For clarity, the terms set forth in Section 8.2(d) must be included within the Exercised Product License Agreement and are not subject to arbitration and Ultragenyx shall be required to enter into an Exercised Product License Agreement including those terms if the Takeda Option is exercised pursuant to Section 8.2(c).

8.3 **Takeda Right of First Negotiation on Ultragenyx Pipeline Products.** As additional consideration for the premium being paid by Takeda to Ultragenyx under the Common Stock Purchase Agreement, and notwithstanding anything to the contrary contained in this Agreement, if, during [***] following expiration of the applicable Takeda Option Term, Ultragenyx intends to license (all or a subset of all rights) or otherwise transfer any Ultragenyx Pipeline Product to a Third Party in the Takeda ROFN Territory, Ultragenyx will provide Takeda with prior written notice of such intent and, for a period of [***] after receipt of such notice, Takeda will have a right of first negotiation to enter into a definitive agreement with Ultragenyx for such license (of all or a subset of all rights) or other transfer in the Takeda ROFN Territory. If the Parties fail to enter into a definitive agreement prior to the expiration of [***], Ultragenyx will have the right to enter into a definitive agreement with a Third Party for the license (of all or a subset of all rights) or other transfer of such Ultragenyx Pipeline Product in the Takeda ROFN Territory.

8.4 **Transition of Responsibilities After Exercise of the Takeda Option**. Ultragenyx shall, in accordance with a transition plan set forth in the Exercised Product License Agreement, transfer to Takeda all activities and responsibilities related to the Exercised Products in the Exercised Countries. The Parties shall exercise Commercially Reasonable Efforts to complete the transfer in accordance with such transition plan. Any dispute between the Parties regarding the transition shall be resolved as set forth in the Exercised Product License Agreement.

8.5 **Development and Commercialization After Exercise of the Takeda Option**. After exercise of the Takeda Option, Takeda will use Commercially Reasonable Efforts to Exploit the Exercised Products in the Takeda Option Field in the Exercised Countries at its sole cost and expense; provided, however, notwithstanding the above, Takeda's financial commitment toward global Development costs for Licensed Option Products and an Ultragenyx Pipeline Products will be in accordance with the terms set forth in Section 8.6.

8.6 **Cost Sharing for Development Activities in Takeda Territory**. After exercise of the Takeda Option with respect to a Licensed Option Product and/or an Ultragenyx Pipeline Product:

(a) the Parties will share the costs of future global Development activities for such Licensed Option Product or Ultragenyx Pipeline Product, as applicable, including costs for Clinical Trials and clinical drug supply and chemistry, manufacturing and controls-related activities in accordance with mutually agreed upon Development plans, budgets and cost sharing structures; provided that Takeda shall only be required to share global Development costs where the Development activities are necessary or reasonably useful to support the Development, Regulatory Approval and Commercialization of such product in the Takeda Territory, in which case Takeda will contribute [***]. For clarity, Takeda will not be required to share in the costs of future global Development activities where the Development activities, including Clinical Trials, are not necessary and are not used to support the Development,
Regulatory Approval and Commercialization of such product in the Takeda Territory; and

(b) Notwithstanding the foregoing, Takeda shall be solely responsible for all Development costs where the Development activities are required specifically and solely for Regulatory Approval of a Licensed Option Product or Ultragenyx Pipeline Product, as applicable, in the Takeda Territory. If such Development activities are also necessary or reasonably useful for Regulatory Approval of a Licensed Product, Licensed Option Product or Ultragenyx Pipeline Product, as applicable, outside the Takeda Territory, the Parties will negotiate in good faith to agree upon an equitable sharing of costs for such Development activities.

ARTICLE 9 – REGULATORY

9.1 **Lead Regulatory Party**. Primary regulatory responsibility under this Agreement shall be assigned to one of the Parties (such Party, the "Lead Regulatory Party") as set forth in this Section 9.1.

(a) Ultragenyx shall be the Lead Regulatory Party for all Licensed Products until expiration of the [***] Option Term. Following expiration of the [***] Option Term, whether or not Ultragenyx has exercised the [***] Option (i) Takeda shall be the Lead Regulatory Party for Licensed [***] Products in the Takeda Field unless otherwise agreed by the Parties, and (ii) Ultragenyx shall be the Lead Regulatory Party for Licensed [***] Products in the Ultragenyx Field and shall be the Lead Regulatory Party for Licensed Analog Products in the Ultragenyx Field.

(b) Ultragenyx shall be the Lead Regulatory Party for all Ultragenyx Pipeline Products in the Territory until expiration of the Takeda Option Term. Following the expiration of the Takeda Option Term, Ultragenyx shall be the Lead Regulatory Party in the Territory for all Ultragenyx Pipeline Products for which the Parties have not entered into an Exercised Product License Agreement. For clarity, at all times Ultragenyx shall be the Lead Regulatory Party for all Ultragenyx Pipeline Products outside of the Takeda Territory. If Takeda exercises the Takeda Option with respect to an Exercised Product, the Exercised Product License Agreement shall provide that Takeda shall be the Lead Regulatory Party for such Exercised Product in the Licensed Field in the Takeda Territory.

(c) The Parties will agree as to which Party shall be the Lead Regulatory Party for the [***] Products and each Candidate Product prior to the expiration of the Collaboration Term; provided, however, that Takeda shall be the Lead Regulatory Party (i) if the Parties are unable to agree, (ii) at any time after Ultragenyx provides Takeda written notice that it will not exercise the Ultragenyx Option with respect to the [***] Products and (iii) for the planned Scientific Advice with the Dutch Medicines Evaluation Board and US Orphan Drug Designation follow-up (as needed) for [***]. Ultragenyx shall be the Lead Regulatory Party for each Option Product for which the Parties have entered into an Option Product License Agreement and Takeda shall be the Lead Regulatory Party for each Option Product for which the Parties have not entered into an Option Product License Agreement.

(d) In accordance with the foregoing, upon entering into an Option Product License Agreement or Exercised Product License Agreement, it is understood that the terms of such Option Product License Agreement or Exercised Product License Agreement will govern with respect to such Option Product covered by such Option Product License Agreement or Exercised Product covered by such Exercised Product License Agreement, as applicable.

9.2 **Initial Transfer of Data and Regulatory Materials**.

(a) **Transfer to Ultragenyx**

(i) As soon as practicable after the Effective Date, but in any event no later than sixty (60) days after the Effective Date, Takeda shall timely transfer to Ultragenyx copies of (A) all Regulatory Materials (in electronic or other format) in its possession related to the use of the Licensed [***] Products in the Ultragenyx Field (and, solely for purposes of Ultragenyx's performance of its obligations under Section 4.3(a)(ii), in the Takeda Field) and (B) the briefing book, FDA meeting minutes, Takeda meeting minutes, and FDA correspondence associated with [***], the US Orphan Drug Designation Request and subsequent regulatory correspondence, and the briefing book and correspondence for Scientific Advice with the Dutch Medicines Evaluation Board, in each case for the [***] Products in the Licensed Field and existing as of such date of transfer. Following each such transfer and at a time to be mutually agreed by the Parties, the Parties shall take all steps necessary (a) for Ultragenyx to own or have the right of reference to the INDs and Regulatory Approvals necessary to conduct Development of the Licensed [***] Product in the Ultragenyx Field and (b) for Takeda to own or have the right of reference to the INDs and Regulatory Approvals necessary to conduct Development of the Licensed [***] Product in the Takeda Field.

(ii) Within sixty (60) days after the Effective Date, Takeda shall make available to Ultragenyx separate copies (in electronic or other format) of the study reports from all non-clinical trials and Clinical Trials in the Territory, in each case, whether completed as of the Effective Date or then in-progress, that are Controlled by Takeda (to the extent not previously provided to Ultragenyx), as such reports become available to Takeda, and to the extent that they relate to the use of the Licensed [***] Products for the Territory.

(b) **Transfer to Takeda**

(i) As soon as practicable after the effective date of an Exercised Product License Agreement for a given Exercised Product, but in any event no later than sixty (60) days after such date, Ultragenyx shall timely transfer to Takeda copies of all Regulatory Materials (in electronic or other format) in its possession related to the use of the Exercised Product in the Exercised Countries and which support the Product INDs, the Product Regulatory Approvals and associated correspondence, existing as of such date of transfer. Promptly after such transfer, Ultragenyx shall take all steps necessary to transfer ownership of all such Product INDs and Product Regulatory Approvals in the Takeda Territory to Takeda, including, if applicable, submitting to the PMDA a letter or other necessary documentation (with a copy to Takeda) notifying the PMDA of the transfer of such ownership. From time to time after the IND Date, and solely to the extent not previously disclosed, Ultragenyx shall, and shall cause its Affiliates to, without additional compensation, disclose and make available to Takeda, in whatever form Takeda may reasonably request, all Regulatory Materials Controlled by Ultragenyx and related to the use of an Exercised Product in the Exercised Countries.

(ii) Within sixty (60) days after the Parties enter into an Exercised Product License Agreement for a given Exercised Product, Ultragenyx shall make available to Takeda separate copies (in electronic or other format) of the study reports from all non-clinical trials and Clinical Trials in the Territory, in each case, whether completed as of the Effective Date, that are Controlled by Ultragenyx (to the extent not previously provided to Takeda), as such reports become available to Ultragenyx, and to the extent that they relate to the use of the Exercised Products in the Exercised Countries.

9.3 **Preparation of Regulatory Materials**.

(a) After the Effective Date (or, as applicable, the IND Date), the Lead Regulatory Party shall have the sole right and responsibility, and shall exercise Commercially Reasonable Efforts, to prepare, obtain, and maintain, as applicable, the Regulatory Materials, including the Product INDs, the Product Regulatory Approvals, and other submissions, and to conduct communications with the FDA, for the relevant Products in the applicable indication in the Territory or applicable portion thereof, except in the case of Licensed [***] Products from the Effective Date until expiration of the [***] Option Term, during which time Takeda shall hold the IND and Ultragenyx (i.e., the Lead Regulatory Party) shall receive a right of reference from Takeda. Except with respect to Licensed [***] Products from the Effective Date until expiration of the [***] Option Term, all Product INDs and Product Regulatory Approvals generated after the Effective Date, including any supplements or amendments to those Product INDs and Product Regulatory Approvals in existence as of the Effective Date, with respect to such Products in the

applicable indication in the Territory or applicable portion thereof under this Agreement shall be owned by, and shall be the sole property and held in the name of, Lead Regulatory Party or its designee.

(b) Other than the Scientific Advice Briefing Book for the [***] Products which has been prepared as of the Execution Date but not yet been submitted, the Lead Regulatory Party shall provide the other Party with an opportunity to review and comment on all material Regulatory Materials submitted by the Lead Regulatory Party to a Regulatory Authority after the Effective Date, in each case reasonably in advance of when the Lead Regulatory Party intends to submit such Regulatory Materials to the applicable Regulatory Authority. The other Party shall provide its comments within [***], or such other period of time mutually agreed to by the Parties. The Lead Regulatory Party shall consider in good faith any such comments of the other Party. The Lead Regulatory Party shall provide the other Party with a copy in electronic form of all material Regulatory Materials filed with the Regulatory Authority related to the use of the relevant Products.

(c) The Lead Regulatory Party shall notify the other Party within no less than [***] of any request for a meeting or substantive telephone conference call with a Regulatory Authority with respect to any Product IND or Product Regulatory Approval. Upon the other Party's request, the Lead Regulatory Party shall request that the FDA or other Regulatory Authority permit at least [***] of the other Party's employees to attend any such meeting or conference call. To the extent permitted by the FDA or other Regulatory Authority, the other Party shall have the right to participate in any such meeting or conference call. The foregoing rights and obligations apply with respect to meetings or conferences initiated by the Lead Regulatory Party or by a Regulatory Authority. The Lead Regulatory Party shall promptly furnish the other Party with copies of all substantive correspondence related to the relevant Product the Lead Regulatory Party has had with the Regulatory Authority, and contact reports concerning substantive conversations or minutes from any substantive meetings with a Regulatory Authority related to such Product.

(d) Notwithstanding the foregoing, Takeda, in consultation with Ultragenyx, shall be responsible for the preparation of any components of Regulatory Materials to be filed by Ultragenyx that relate to the Manufacture of a Licensed Product or Option Product. Takeda shall use Commercially Reasonable Efforts to prepare such components in a timely manner and provide such components to Ultragenyx with sufficient time for Ultragenyx to review and comment on such components; provided, however, that Takeda may use an alternative arrangement (such as a drug master file) to preserve the confidentiality of such components to the extent required by any Third Party agreements or, in Takeda's reasonable discretion, if otherwise necessary to protect Takeda confidential information and such alternative arrangement is permissible under Applicable Laws; provided, further, that if Ultragenyx reasonably requests additional information with respect to the Development or Commercialization of a Licensed Product or Option Product otherwise treated as confidential in such alternative arrangement (such as a drug master file), Takeda shall reasonably consider such request. In the event that Ultragenyx elects to Manufacture a Licensed Product or Option Product, Ultragenyx shall notify Takeda of such election and, to the extent covered by the license rights granted in Sections 3.1(a)

and 3.1(c) (for Licensed Products) or Section 6.5(a) (for Option Products), Takeda shall promptly transfer to Ultragenyx or its Third Party designee all Regulatory Materials, processes and technical information Controlled by Takeda or its Affiliates that are reasonably necessary and useful for the Manufacture of such Licensed Product or Option Product, and thereafter Ultragenyx shall be responsible for the preparation of any components of Regulatory Materials to be filed related to the Manufacture by Ultragenyx or its Third Party designee of such Licensed Product or Option Product.

9.4 **Cooperation, Consultation and Review**.

(a) The Parties shall cooperate with each other to achieve the regulatory objectives contemplated herein in a timely, accurate and responsive manner and shall assist the other Party as reasonably requested in connection with the preparation and filing of Regulatory Materials in the Licensed Field, whether in or outside of the Territory. The Parties shall establish a joint regulatory working group to manage Licensed Product regulatory activities and issues. It is the intention of the Parties that the joint regulatory working group shall meet (in person or via teleconference) on an as-needed basis after the Effective Date and throughout the Term, but at a minimum on a quarterly basis. The Parties agree and acknowledge that the activities of Ultragenyx with respect to (i) Licensed [***] Products in the Ultragenyx Field and (ii) Licensed Analog Products in the Licensed Field and the activities of Takeda with respect to (A) Licensed [***] Products in the Takeda Field and (B) Licensed Products outside of the Licensed Field, shall be coordinated such that they are consistent with the overall objective of facilitating Regulatory Approvals.

(b) The other Party shall assist the Lead Regulatory Party, as is reasonably necessary, in order for the Lead Regulatory Party to obtain and maintain the Product INDs and the Product Regulatory Approvals, including in connection with the preparation and filing of Regulatory Materials necessary to maintain such Product INDs and Product Regulatory Approvals.

9.5 **Regulatory Costs and Expenses**. Each Party shall bear its own costs and expenses incurred related to the preparation, maintenance, formatting and filing of the Regulatory Materials.

9.6 **Rights of Reference to Regulatory Materials**. Each Party hereby grants to the other Party a right of reference to all Regulatory Materials, including any data relied on in support of such Regulatory Materials, solely for the purpose of seeking, obtaining and maintaining Regulatory Approvals for the Products, consistent with the roles of the Parties set forth in this Agreement.

9.7 **Labeling Information Exchange/Labeling Agreement**. The Parties shall cooperate to develop methods and/or procedures for sharing information related to Labeling. Specific details regarding the management of Labeling information, including CCDS will be delineated in a separate Labeling agreement that shall be agreed upon by the Parties.

9.8 **Adverse Event Reporting and Safety Data Exchange**.

(a) **Safety Information Exchange; Pharmacovigilance Agreement**.

(i) The Parties shall cooperate to develop methods and/or procedures for sharing information relating to the clinical experiences in accordance with safety reporting requirements of the respective Regulatory Authorities and as necessary for a Party to comply with Applicable Laws. Specific details regarding the management of safety information including adverse events reports related to the Development and the Commercialization of the Products will be delineated in a separate global pharmacovigilance agreement (the "PVA") that shall be agreed to by the Parties as soon as reasonably practicable, but in any event not later than [***] of the Effective Date. The Lead Regulatory Party shall be responsible for the compliance and filing of all required safety reports to the Regulatory Authorities in the Territory, including annual safety reports, throughout the Term.

(ii) The PVA shall provide as follows:

(A) Unless otherwise agreed by the Parties, the Lead Regulatory Party shall maintain the global safety database for the Products, and mirror databases will be maintained by the other Party; provided, however, that Takeda shall maintain the global safety database regarding Licensed [***] Products, and Ultragenyx shall maintain the global safety database regarding Licensed Analog Products. For clarity, to the extent a Party is no longer actively Developing or Commercializing a Licensed [***] Product, then the global safety database shall be transferred to the Party that continues to actively Develop or Commercialize such Licensed [***] Product.

(B) Each Party shall timely report to the other Party all clinical experiences, safety monitoring, and pharmacovigilance surveillance observed in the Territory, which in all cases shall be (i) for clinical studies: as soon as practicable, [***] and (ii) for commercial Products: [***]; exchange of information shall be on a Council for International Organizations of Medical Sciences Suspect Adverse Reaction Report Form ("CIOMS Form").

(C) The other Party shall prepare and provide to the Lead Regulatory Party on a timely basis safety updates in order for the Lead Regulatory Party to meet the safety report submission requirements necessary to maintain the Product INDs and the Product Regulatory Approvals.

(b) **Regulatory Reporting of Safety Information**. The Parties shall work together to achieve consensus with respect to safety issues related to the Products, including urgent safety information, and to report said opinion to safety boards, investigators, and to applicable Regulatory Authorities. In the event that, after reasonable medical and scientific consultation, the Parties cannot achieve consensus with respect to safety issues to be reported to any applicable Regulatory Authority, the Lead Regulatory Party shall have final decision making

authority with respect to the Products in the Licensed Field in the Territory. Notwithstanding anything to the contrary in this Agreement, either Party may report safety matters to a Regulatory Authority that it reasonably determines are necessary to report prior to the conclusion of the dispute resolution procedure.

9.9 **Regulatory Authority Communications Received by a Party**. Each Party shall inform the other Party in a timely manner, not to exceed [***], of the notification of any action by, or notification or other information which it receives (directly or indirectly) from any Regulatory Authority which: (i) raises any material concerns regarding the safety or efficacy of a Product; (ii) indicates or suggests a potential material liability of either Party to Third Parties in connection with a Product; (iii) is reasonably likely to lead to a recall or market withdrawal of a Product; or (iv) relates to expedited reports of adverse events with respect to a Product, or Product Complaints, and which may have a material impact on obtaining or maintaining Regulatory Approval or the continued Commercialization of a Product, as then conducted. The other Party will fully cooperate with and assist such Party in complying with regulatory obligations and communications, including by providing to such Party, in a timely manner after a request, such information and documentation in the other Party's possession as may be necessary or helpful for the Party to prepare a response to an inquiry from a Regulatory Authority. Each Party will provide the other Party in a timely manner with a copy of all correspondence received from a Regulatory Authority specifically regarding the matters referred to above.

9.10 **Audit**. If a Regulatory Authority desires to conduct an inspection or audit of a Party's facility or a facility under contract with such Party with regard to a Product in the Territory, then the audited Party shall notify the other Party as soon as practicably possible after receipt of such notification of such audit or inspection and provide copies of any materials provided to it by the applicable Regulatory Authority; provided, that the audited Party shall not be required to notify the other Party of audits or inspections that are of a routine nature or that do not relate to a Product, except where such audits result in communications or actions of such Regulatory Authority which have a direct impact upon a Product. In addition, if a Regulatory Authority conducts an unannounced inspection or audit of a Party's facility or a facility under contract with such Party with regard to a Product in the Territory, then the audited Party shall notify the other Party within [***] of commencement of such audit or inspection. The audited Party shall cooperate, and shall use reasonable efforts to cause the contract facility to cooperate, with such Regulatory Authority and the other Party during such inspection or audit. Following receipt of the inspection or audit observations of such Regulatory Authority (a copy of which the audited Party will immediately provide to the other Party), the audited Party will also provide the other Party with copies of any written communications received from Regulatory Authorities with respect to such facilities in a timely manner after receipt, to the extent such written communications relate directly to a Product or the Manufacture thereof, and will prepare the response to any such observations. The audited Party will provide the other Party with a copy of any proposed response to such communications and will consider in good faith such other Party's reasonable comments with respect to such proposed response. The audited Party agrees to conform its activities under this Agreement to any commitments made in such a response.

9.11 **Recalls and Voluntary Withdrawals**. Each Party shall notify the other Party promptly but in no event later than [***] following its determination that any event, incident, or circumstance has occurred that may result in the need for a recall, market suspension, or market withdrawal of a Product under any MAA or Regulatory Approval for the Product held by such Party and filed with Regulatory Authorities in the Territory, and shall include in such notice the reasoning behind such determination, and any supporting facts. Such Party shall have the sole right to make the final determination whether to voluntarily implement any such recall, market suspension, or market withdrawal in the Territory; provided that prior to any implementation of such a recall, market suspension, or market withdrawal, the such Party shall, to the extent practical, consult with the other Party and shall consider the other Party's comments in good faith. For all recalls, market suspensions or market withdrawals undertaken pursuant to this Section 9.11, such Party shall be solely responsible for the execution thereof, and the other Party shall reasonably cooperate in all such recall efforts. Subject to ARTICLE 17, such Party shall be responsible for all costs of any such recall, market suspension, or market withdrawal; provided that, the other Party shall be responsible for the costs of any recall, market suspension, or market withdrawal with respect to a Product in the Territory to the extent such recall, market suspension, or market withdrawal is attributable to the other Party's breach of its obligations hereunder or its negligence, recklessness or willful misconduct.

ARTICLE 10 – MANUFACTURING AND SUPPLY

10.1 **Supply Agreement**. The Parties shall enter into mutually agreeable supply agreements as soon as appropriate after the Effective Date covering the manufacture and research supply (other than as provided in Section 6.6), clinical supply or Commercial supply of Compounds or Products needed for Development or Commercialization.

ARTICLE 11 – PAYMENT

11.1 **Licensed Product Development Milestones Payable to Takeda**.

(a) Ultragenyx shall pay to Takeda a milestone payment within forty-five (45) days after the first achievement of each of the following milestones for each Licensed Product, calculated as follows:

(i) [***];

(ii) [***];

(iii) [***]

(iv) [***];

(v) [***]; and

(vi) [***]

(b) Each milestone payment in this Section 11.1 shall be payable only upon the first achievement of such milestone for each Licensed Product and no amounts shall be due for subsequent or repeated achievements of such milestone for the same Licensed Product.

11.2 **Licensed Product Sales Milestones Payable to Takeda**.

(a) Ultragenyx shall pay to Takeda a milestone payment within [***] after the first achievement of each of the following milestones for the aggregated annual Net Sales of all Licensed Products, calculated as follows:

(i) upon the Net Sales in the Territory of all Licensed Products made by Ultragenyx, its Affiliates and Sublicensees in a given Calendar Year equaling or exceeding [***];

(ii) upon the Net Sales in the Territory of all Licensed Products made by Ultragenyx, its Affiliates and Sublicensees in a given Calendar Year equaling or exceeding [***]; and

(iii) upon the Net Sales in the Territory of all Licensed Products made by Ultragenyx, its Affiliates and Sublicensees in a given Calendar Year equaling or exceeding [***].

(b) Each milestone payment in this Section 11.2 shall be payable only upon the first achievement of such milestone for all Licensed Products in aggregate and no amounts shall be due for subsequent or repeated achievements of such milestone. If two or more milestone events are achieved in the same Calendar Year, Ultragenyx shall pay to Takeda each milestone payment corresponding to the respective milestone event.

11.3 **Licensed Product Royalties Payable to Takeda.** Subject to Section 11.8 below, and during the applicable Licensed Product Royalty Term, Ultragenyx shall pay to Takeda, on a Licensed Product-by-Licensed Product basis, a running royalty at the following incremental royalty rates, on Net Sales of each Licensed Product in the Territory in a Calendar Year:

Net Sales in the Territory	**Royalty Rate**
For that portion of annual Net Sales less than $[***]	[***]%
For that portion of annual Net Sales greater than or	[***]%

equal to $[***] but less than $[***]	
For that portion of annual Net Sales greater than or equal to $[***] but less than $[***]	[***]%
For that portion of annual Net Sales greater than or equal to $[***]	[***]%

11.4 **Exercised Product Milestones and Fees Payable to Ultragenyx**.

(a) Pursuant to the applicable Exercised Product License Agreement, Takeda shall pay to Ultragenyx a milestone payment of [***] within [***] after the first Regulatory Approval in the first indication in Japan for [***] if such product is an Exercised Product that has not been terminated at the time of such Regulatory Approval. The milestone payment in this Section 11.4(a) shall be payable only upon the first achievement of such milestone for each such Exercised Product and no amounts shall be due for subsequent or repeated achievements of such milestone for such Exercised Product. For clarity, the maximum aggregate amount payable by Takeda for each Exercised Product pursuant to this Section 11.4(a) is [***].

(b) For all Ultragenyx Pipeline Products other than [***], during the Takeda Option Negotiation Period for such Ultragenyx Pipeline Products, the Parties will negotiate in good faith (for inclusion in the applicable Exercised Product License Agreement) commercially reasonable financial terms in addition to the royalties contemplated in Section 11.6 (such as one or more of the following: option exercise fees, sales and development milestones, reimbursement for historical research and development costs allocable to Japan, and milestones due to Third Party licensors) for such Ultragenyx Pipeline Products, taking into consideration factors such as the investment in the collaboration under this agreement already made by Takeda, including the premium paid by Takeda to Ultragenyx under the Common Stock Purchase Agreement. If the Parties cannot reach agreement on such commercially reasonable financial terms during the Takeda Option Negotiation Period, either Takeda or Ultragenyx may seek a final decision regarding the commercially reasonable financial terms pursuant to binding arbitration as set forth in Section 16.3.

11.5 **Licensed Product Royalties Payable to Ultragenyx for the Exercised Countries**. Subject to Section 11.8 below, and during the applicable Licensed Product Royalty Term, pursuant to the applicable Exercised Product License Agreement, Takeda shall pay to Ultragenyx, on a Licensed Product-by-Licensed Product basis, a running royalty at the following incremental royalty rates, on aggregate, Net Sales of each Exercised Product that is a Licensed Product in the Exercised Countries in a Calendar Year:

(a) If the Takeda Option for such Licensed Product is exercised by Takeda prior to Takeda's receipt of the Final Phase II Data Package for such Licensed Product:

Net Sales in the Exercised Countries	Royalty Rate
For that portion of annual Net Sales less than $[***]	[***]%
For that portion of annual Net Sales greater than or equal to $[***] but less than $[***]	[***]%
For that portion of annual Net Sales greater than or equal to $[***] but less than $[***]	[***]%
For that portion of annual Net Sales greater than or equal to $[***]	[***]%

(b) If the Takeda Option for such Licensed Product is exercised by Takeda after Takeda's receipt of the Final Phase II Data Package for such Licensed Product:

Net Sales in the Exercised Countries	Royalty Rate
For that portion of annual Net Sales less than $[***]	[***]%
For that portion of annual Net Sales greater than or equal to $[***] but less than $[***]	[***]%
For that portion of annual Net Sales greater than or equal to $[***] but less than $[***]	[***]%
For that portion of annual Net Sales greater than or equal to $[***]	[***]%

11.6 **Licensed Option Product and Ultragenyx Pipeline Product Royalties Payable to Ultragenyx for the Exercised Countries**. During the Takeda Option Negotiation Period for a Licensed Option Product or Ultragenyx Pipeline Product, the Parties will negotiate in good faith (for inclusion in the applicable Exercised Product License Agreement) tiered royalty rates on annual Net Sales of such Licensed Option Product or Ultragenyx Pipeline Product to be paid by Takeda to Ultragenyx during the Takeda Royalty Term. If the Parties cannot reach agreement on such tiered royalty rates during the Takeda Option Negotiation Period, either Takeda or Ultragenyx may seek a final decision regarding the royalty rates pursuant to binding arbitration as set forth in Section 16.3.

11.7 **Royalty Reduction for Generic Product Entry in a Country**. On a Licensed Product- by-Licensed Product basis, the royalty rates set forth in Sections 11.3 and 11.5 for Net Sales of a Product in a country shall be reduced by [***] in each Calendar Quarter during which the Generic Competition Percentage with respect to such Licensed Product in such country in such Calendar Quarter is greater than or equal to [***].

11.8 **Payment for Third Party Licenses**.

(a) Each Party will be responsible for paying all Third Party license fees, royalties, and/or milestones, with respect to Third Party licenses entered into by such Party or its Affiliates prior to or on the Effective Date or during the Term, for intellectual property that is necessary or reasonably useful for the Exploitation of any Licensed Product. For such Third Party licenses to Preexisting Third Party IP, the paying Party will be entitled to deduct up to [***] of such amounts due to any such Third Party from royalties payable to the other Party hereunder on such Licensed Product. For such Third Party licenses obtained during the Term, the paying Party will be entitled to deduct [***] of such amounts due to any such Third Party from royalties payable to the other Party hereunder on such Licensed Product. Notwithstanding the foregoing, in no event shall such royalty payable to Takeda in any Calendar Quarter as a result of this reduction be less than [***] of the amount that would otherwise be due.

(b) Ultragenyx shall be responsible for paying all Third Party license fees, royalties, and/or milestones, with respect to Third Party licenses for intellectual property that is necessary or reasonably useful for the Exploitation of any Ultragenyx Pipeline Product, where such licenses are entered into (i) prior to or on the Effective Date or (ii) unless and until such Ultragenyx Pipeline Product is an Exercised Product, during the Term. Each Party will be responsible for paying all Third Party license fees, royalties, and/or milestones, with respect to Third Party licenses for intellectual property that is necessary or reasonably useful for the Exploitation of any Ultragenyx Pipeline Product that is an Exercised Product entered into by such Party or its Affiliates on or after the date on which it becomes an Exercised Product. For such Third Party licenses obtained by Takeda or its Affiliates, Takeda will be entitled to deduct [***] of such amounts due to any such Third Party from royalties payable to Ultragenyx on such Exercised Product. Notwithstanding the foregoing, in no event shall the royalty payable to Ultragenyx in any Calendar Quarter on such Exercised Product as a result of this reduction be less than [***] of the amount that would otherwise be due.

(c) Notwithstanding the foregoing, for intellectual property held by a Third Party that is necessary or reasonably useful for the Exploitation of any Exercised Products in both the Exercised Countries and other countries in the Territory, the Parties will coordinate license negotiations with such Third Party for rights in both the Exercised Countries and other countries in the Territory.

11.9 **Manner of Royalty Payment.** Each Party will calculate and report royalty payments due by such Party to the other Party under Section 11.3 or 11.5, as applicable, each Calendar Quarter. Each Party shall pay all royalty payments due under Section 11.3 or 11.5, as applicable, within sixty (60) days after the end of each Calendar Quarter and shall include with each payment a report containing the following information for the applicable Calendar Quarter: (a) the amount of gross sales (in U.S. dollars) of the Products in the Territory; (b) an itemized calculation of Net Sales in the Territory showing deductions, to the extent applicable, provided for in the definition of "Net Sales"; (c) a calculation of the royalty payment due on such sales;
(d) an accounting of the number of units and prices for the Products sold; and (e) application of

the reductions, if any, made in accordance with the terms of Section 11.7 and 11.8. Within twenty (20) Business Days after the end of each Calendar Quarter, each Party shall provide a preliminary report as described above for the most recent Calendar Quarter then ended. Each Party shall reasonably cooperate to reconcile any deviations and confirm the accuracy to the extent necessary under Applicable Laws, GAAP or IFRS.

11.10 **Exchange Rate**. The rate of exchange to be used in computing the amount of currency equivalent in U.S. Dollars owed to a Party under this Agreement shall be equal to the weighted average exchange rate, over the applicable Calendar Quarter, between each currency of origin and U.S. Dollars as reported by OANDA (www.oanda.com), or an equivalent resource as agreed by the Parties, on the last Business Day of the Calendar Quarter in which the applicable Net Sales were made.

11.11 **Taxes**

(a) **Cooperation and Coordination**. The Parties acknowledge and agree that it is their mutual objective and intent to appropriately calculate, to the extent feasible and legal, taxes payable with respect to their collaborative efforts under this Agreement and that they shall use all commercially reasonable efforts to cooperate and coordinate with each other to achieve such objective. Ultragenyx shall cooperate with Takeda in seeking any tax exemption or credits that may be available to Takeda with respect to any research which Takeda or its affiliates perform or fund under this Agreement, including any credits under section 45C of the U.S. Internal Revenue Code of 1986, as amended.

(b) **Payment of Tax**. A Party receiving a payment pursuant to this ARTICLE 11 shall pay any and all taxes levied on such payment. A Party making a payment pursuant to this ARTICLE 11 shall make a reasonable effort to obtain the lowest tax rate under Applicable Laws for taxes required to be deducted and withheld. If Applicable Laws require that taxes be deducted and withheld from a payment made pursuant to this ARTICLE 11, after a Party making a payment makes a reasonable effort to obtain the lowest tax rate, the remitting Party shall: (i) deduct those taxes from the payment; (ii) pay the taxes to the proper taxing authority; and (iii) send evidence of the obligation together with proof of payment to the other Party within sixty (60) days following that payment.

(c) **Tax Residence Certificate**. A Party receiving a payment pursuant to this ARTICLE 11 shall provide the remitting Party appropriate certification from relevant revenue authorities that such Party is a tax resident of that jurisdiction, if such receiving Party wishes to claim the benefits of an income tax treaty to which that jurisdiction is a party. Upon the receipt thereof, any deduction and withholding of taxes shall be made at the appropriate treaty tax rate.

(d) **Assessment**. Either Party may, at its own expense, protest any assessment, proposed assessment, or other claim by any Governmental Authority for any additional amount of taxes, interest or penalties or seek a refund of such amounts paid if permitted to do so by Applicable Laws. The Parties shall cooperate with each other in any protest by providing records and such additional information as may reasonably be necessary for a Party to pursue such protest.

(e) **Withholding**. If a Party that owes a payment under this Agreement assigns its rights and obligations to any Person and if, solely as a result of such assignment, the withholding or deduction of tax required by Applicable Laws with respect to payments under this Agreement is increased, then, subject to Section 11.11(f), any amount payable under this Agreement shall be increased to take into account such withheld or deducted taxes as may be necessary so that, after making all required withholdings and deductions (including withholdings and deductions on amounts payable under this Section 11.11(e)), the payee receives an amount equal to the sum it would have received had no such increased withholding or deduction been made. For the avoidance of doubt, if a payee under this Agreement assigns its rights and obligations under this Agreement, the payee shall not be entitled to any additional payments with respect to Taxes arising as a result of such payee's assignment.

(f) **Credit.** To the extent a payee obtains any credit for Taxes for which it has received a payment pursuant to Section 11.11(e) against any liability for tax in the year in which the receipt is taxable, any preceding years, or any succeeding years within the term of this Agreement, thereby reducing out-of-pocket tax payments by the Section 11.11(e)-payee in such year or years, calculated on a "with and without" basis, the Section 11.11(e)-payee shall promptly reimburse the Section 11.11(e)-payor an amount equal to its tax savings resulting from such credit and the Section 11.11(e)-payee shall timely provide the Section 11.11(e)-payor with reasonable evidence as may reasonably be requested to determine whether any amounts are subject to reimbursement pursuant to this Section 11.11(f).

11.12 **Audit.** Each Party will maintain complete and accurate records in sufficient detail to permit the other Party to confirm the accuracy of the calculation of royalty and other payments under this Agreement. Upon reasonable prior notice, such records shall be available during regular business hours for a period of three (3) years from the end of the Calendar Year to which they pertain for examination at the expense of the requesting Party, and not more often than once each Calendar Year, by an independent certified public accountant selected by the requesting Party and reasonably acceptable to the other Party, for the sole purpose of verifying the accuracy of the financial reports furnished by the other Party pursuant to this Agreement. Any such auditor shall not disclose the other Party's Confidential Information, except to the extent such disclosure is necessary to verify the accuracy of the financial reports furnished by the other Party or the amount of payments due by the other Party under this Agreement during the prior thirty six (36) months. Any amounts shown to be owed but unpaid shall be paid within thirty (30) days from the accountant's report, plus interest (as set forth in Section 11.13) from the original due date. Any amounts shown to have been overpaid shall be refunded within thirty (30) days from the accountant's report. The requesting Party shall bear the full cost of such audit unless such audit discloses an underpayment by other Party of more than five percent (5%) of the amount due, in which case the other Party shall bear the full cost of such audit.

11.13 **Manner of Payment, Late Payment.** All payments due to a Party hereunder shall be made in U.S. Dollars by wire transfer of immediately available funds into an account designated by such Party. If a Party does not receive payment of any sum due to it on or before the due date, simple interest shall thereafter accrue on the sum due to such Party until the date of payment at the per annum rate of one percent (1%) over the then-current prime rate quoted by

Citibank in New York City or the maximum rate allowable by Applicable Laws, whichever is lower.

11.14 **Finance and Accounting Working Group**. The Parties shall cooperate with each other to achieve the finance and accounting objectives contemplated herein in a timely, accurate and responsive manner. The Parties shall establish a finance and accounting working group to manage financial and accounting affairs related to the Products, which, for at least the first twelve (12) months after the Effective Date, shall meet monthly unless otherwise agreed upon by the Parties.

ARTICLE 12 – INTELLECTUAL PROPERTY MATTERS

12.1 **Ownership of Inventions**.

(a) **Sole Ownership.** Subject to the terms of this Agreement, each Party shall own any Inventions made solely by its own employees, agents, or independent contractors or its Affiliate's or sublicensees' employees, agents, or independent contractors in the course of conducting its activities under this Agreement, together with all intellectual property rights therein.

(b) **Joint Ownership**. The Parties shall jointly own any Inventions that are made jointly by employees, agents, or independent contractors of each Party or its Affiliates in the course of performing activities under this Agreement, together with all intellectual property rights therein (the "Joint Inventions").

(c) **Inventorship.** For purposes of this Agreement, inventorship shall be determined in accordance with U.S. patent laws.

12.2 **Assignment Obligation and Disclosure of Inventions**.

(a) Each Party shall cause all Persons who perform activities for such Party under this Agreement to be under an obligation to assign (or, if such Party is unable to cause such Person to agree to such assignment obligation despite such Party using commercially reasonable efforts to negotiate such assignment obligation, provide a license under) their rights in any Information and Inventions resulting therefrom to such Party, except where Applicable Law requires otherwise and except in the case of governmental, not-for-profit and public institutions which have standard policies against such an assignment (in which case a suitable license, or right to obtain such a license, shall be obtained).

(b) Takeda will promptly disclose to Ultragenyx in writing, the conception, discovery, development or making of any Joint Inventions and any Inventions Covering Ultragenyx Pipeline Improvements by Persons who perform activities for Takeda under this Agreement.

(c) Ultragenyx will promptly disclose to Takeda in writing the conception, discovery, development or making of any Joint Inventions and any Inventions Covering Licensed Product Improvements, or Option Product Improvements.

(d) Each Party will promptly disclose to the other Party in writing, the conception, discovery, development or making of any Joint Inventions by Persons who perform activities for it under this Agreement.

12.3 **Prosecution of Patents.**

(a) **Licensed** [***] **Patents, Licensed Product Improvement Patents, and Joint Patents relating to Licensed Products.** Except as otherwise provided in this Section 12.3(a), as between the Parties, Takeda shall have the sole right and authority to prepare, file, prosecute and maintain the Licensed [***] Patent, Licensed Product Improvement Patents, and, where relating to Licensed Products, Joint Patents (collectively, the "[***] Patent Prosecution") on a worldwide basis (including the right to defend in patent office proceedings such as inter partes reviews, post grant reviews and oppositions).Takeda shall bear all costs of preparation, filing, prosecution and maintenance of the [***] Patent Prosecution in the Territory. Provided that Ultragenyx's rights with respect to the applicable Licensed Product have not terminated, Takeda, upon Ultragenyx's request, shall provide Ultragenyx a reasonable opportunity to review and comment on material communications from any patent authority in the Territory regarding the [***] Patent Prosecution and drafts of any material filings or responses to be made to such patent authorities in advance of submitting such filings or responses. Takeda shall consider Ultragenyx's comments regarding such communications and drafts in good faith with a view to maximizing the Patent protection and scope in the Territory in the Ultragenyx Field. If Ultragenyx's rights with respect to the applicable Licensed Product have not terminated and Takeda determines in its sole discretion to abandon or not maintain any Licensed [***] Patent, Licensed Product Improvement Patent, or, where relating to Licensed Products, Joint Patent that is being prosecuted or maintained by Takeda in the Territory and that is applicable to the in the Ultragenyx Field, then Takeda shall provide Ultragenyx with written notice of such determination within a period of time reasonably necessary to allow Ultragenyx to determine, in its sole discretion, its interest in such Patent(s) (which notice by Takeda shall be given no later than sixty (60) days prior to the final deadline for any pending action or response that may be due with respect to such Patent(s) with the applicable patent authority). If Ultragenyx provides timely written notice expressing its interest in continuing to support such Patent(s), Ultragenyx shall have the right to pursue the filing or support the continued prosecution or maintenance of such Patents and Takeda shall provide to Ultragenyx, subject to reimbursement of Takeda's out-of-pocket costs, all unpublished patent applications and any other information and documents necessary to permit Ultragenyx to take such action to establish or preserve any such Patents. If Ultragenyx pursues the filing or support of such Patents and Takeda continues to pursue a Licensed [***] Product in the Takeda Field, it shall provide Takeda a reasonable opportunity to review and comment on material communications from any patent authority in the Territory regarding such Patents and drafts of any material filings or responses to be made to such patent authorities in advance of submitting such filings or responses. Ultragenyx shall consider Takeda's comments regarding such communications and drafts in good faith.

(b) **Option Product Patents, Option Product Improvement Patents, and Joint Patents Relating to Research Products.** Except as otherwise provided in this Section 12.3(b), as between the Parties, Takeda shall have the sole right and authority to prepare, file, prosecute and maintain the Option Product Patents, Option Product Improvement Patents and, where relating to Research Products, Joint Patents on a worldwide basis (including the right to defend in patent office proceedings such as inter partes reviews, post grant reviews and oppositions). Takeda shall bear all costs of preparation, filing, prosecution and maintenance of Option Product Patents, Option Product Improvement Patents and, where relating to Research Products, Joint Patents in the Territory. During the Collaboration Term, Takeda, upon Ultragenyx's request, shall provide Ultragenyx a reasonable opportunity to review and comment on material communications from any patent authority in the Territory regarding Option Product Patents, Option Product Improvement Patents and, where relating to Research Products, Joint Patents and drafts of any material filings or responses to be made to such patent authorities in advance of submitting such filings or responses. Takeda shall consider Ultragenyx's comments regarding such communications and drafts in good faith with a view to maximizing the Patent protection and scope in the Territory in the Licensed Field; provided that final decision making authority rests with Takeda. If, during the Collaboration Term, Takeda determines in its sole discretion to abandon or not maintain any Option Product Patent, Option Product Improvement Patent and, where relating to Research Products, Joint Patent that is being prosecuted or maintained by Takeda in the Territory, then Takeda shall provide Ultragenyx with written notice of such determination within a period of time reasonably necessary to allow Ultragenyx to determine, in its sole discretion, its interest in such Patent(s) (which notice by Takeda shall be given no later than sixty (60) days prior to the final deadline for any pending action or response that may be due with respect to such Patent(s) with the applicable patent authority). If Ultragenyx provides timely written notice expressing its interest in continuing to support such Patent(s), Ultragenyx shall have the right to pursue the filing or support the continued prosecution or maintenance of such Patents and Takeda shall provide to Ultragenyx, subject to reimbursement of Takeda's out- of-pocket costs, all unpublished patent applications and any other information and documents necessary to permit Ultragenyx to take such action to establish or preserve any such Patents. If Ultragenyx pursues the filing or support of such Patents, it shall provide Takeda a reasonable opportunity to review and comment on material communications from any patent authority in the Territory regarding such Patents and drafts of any material filings or responses to be made to such patent authorities in advance of submitting such filings or responses. Ultragenyx shall consider Takeda's comments regarding such communications and drafts in good faith. Notwithstanding the foregoing, following the execution of an Option Product License Agreement and/or Exercised Product License Agreement covering an Option Product, the terms of such license agreement(s) shall govern the handling of the preparation, filing, prosecution and maintenance of Patents covering the Option Product(s).

(c) **Ultragenyx Pipeline Patents, Ultragenyx Pipeline Improvement Patents, Ultragenyx** [***] **Patents and Joint Patents Related to Ultragenyx Pipeline Products**. Except as otherwise provided in this Section 12.3(c), as between the Parties, Ultragenyx shall have the sole right and authority to prepare, file, prosecute and maintain the Ultragenyx Pipeline Patents, Ultragenyx Pipeline Improvement Patents, Ultragenyx [***] Patents and, where relating to Ultragenyx Pipeline Products, the Patents included in the Joint Inventions (the "Joint Patents"),

on a worldwide basis (including the right to defend in patent office proceedings such as inter partes reviews, post grant reviews and oppositions). Ultragenyx shall bear all costs of preparation, filing, prosecution and maintenance of Ultragenyx Pipeline Patents, Ultragenyx Pipeline Improvement Patents, Ultragenyx [***] Patents and, where relating to Ultragenyx Pipeline Products, Joint Patents in the Territory. During the Takeda Option Term, Ultragenyx, upon Takeda's request, shall provide Takeda a reasonable opportunity to review and comment on material communications from any patent authority in the Territory regarding Ultragenyx Pipeline Patents, Ultragenyx Pipeline Improvement Patents, Ultragenyx [***] Patents and, where relating to Ultragenyx Pipeline Products, Joint Patents and drafts of any material filings or responses to be made to such patent authorities in advance of submitting such filings or responses. Ultragenyx shall consider Takeda's comments regarding such communications and drafts in good faith with a view to maximizing the Patent protection and scope in the Territory; provided that final decision making authority rests with Ultragenyx. During the Takeda Option Term, if Ultragenyx determines in its sole discretion to abandon or not maintain any Ultragenyx Pipeline Patent, Ultragenyx Pipeline Improvement Patent, Ultragenyx [***] Patent and, where relating to Ultragenyx Pipeline Products, Joint Patent that is being prosecuted or maintained by Ultragenyx in the Takeda Territory, then Ultragenyx shall provide Takeda with written notice of such determination within a period of time reasonably necessary to allow Takeda to determine, in its sole discretion, its interest in such Patent(s) (which notice by Ultragenyx shall be given no later than sixty (60) days prior to the final deadline for any pending action or response that may be due with respect to such Patent(s) with the applicable patent authority). If Takeda provides timely written notice expressing its interest in continuing to support such Patent(s), Takeda shall have the right to pursue the filing or support the continued prosecution or maintenance of such Patents and Ultragenyx shall provide to Takeda, subject to reimbursement of Ultragenyx's out- of-pocket costs, all unpublished patent applications and any other information and documents necessary to permit Takeda to take such action to establish or preserve any such Patents. If Takeda pursues the filing or support of such Patents, it shall provide Ultragenyx a reasonable opportunity to review and comment on material communications from any patent authority in the Territory regarding such Patents and drafts of any material filings or responses to be made to such patent authorities in advance of submitting such filings or responses. Takeda shall consider Takeda's comments regarding such communications and drafts in good faith. Notwithstanding the foregoing, following the execution of an Exercised Product License Agreement covering an Ultragenyx Pipeline Product, the terms of such license agreement shall govern the handling of the preparation, filing, prosecution and maintenance of Patents covering such Ultragenyx Pipeline Product.

(d) **Cooperation in Prosecution**. Each Party shall provide the other Party all reasonable assistance and cooperation in the Patent prosecution efforts provided above in this Section 12.3, including providing any necessary powers of attorney and executing any other required documents or instruments for such prosecution, as well as further actions as set forth below.

(i) The Parties shall respectively prepare, file, maintain and prosecute the Patents as set forth in this Section 12.3. As used herein, "prosecution" of such Patents shall

include all communication and other interaction with any patent office or patent authority having jurisdiction over a patent application in connection with pre-grant proceedings.

(ii) All communications between the Parties relating to the preparation, filing, prosecution or maintenance of the Patents as set forth in this Section 12.3, including copies of any draft or final documents or any communications received from or sent to patent offices or patenting authorities with respect to such Patents, shall be considered Confidential Information and subject to the confidentiality provisions of ARTICLE 14.

12.4 **Patent Term Extensions in the Territory**.

(a) The Parties will discuss and approve for which, if any, of the Patents under this Agreement the Parties should seek Patent Term Extensions in the Territory**.** If the Parties are unable to reach agreement for which, if any, of such Patents the Parties should seek Patent Term Extension, the final decision shall rest with the Party who first receives Regulatory Approval for the Licensed Product or Option Product, as applicable, with respect to which the Patent Term applies for such Party's territory. The Party with final decision-making authority shall act with reasonable promptness in light of the stage of the Products to apply for any such Patent Term Extensions, in accordance with such decision. The Party that does not apply for an extension hereunder will cooperate fully with the other Party in making such filings or actions, including making available all required Regulatory Materials (including underlying data) and Information and executing any required authorizations to apply for such Patent Term Extension. All expenses incurred in connection with activities of each Party with respect to the Patent(s) for which such Party seeks Patent Term Extensions pursuant to this 12.4 shall be entirely borne by the Party applying for such Patent Term Extension.

12.5 **Orange Book Listing**. The Party that is the NDA holder for the applicable Product shall be responsible for listing and maintaining all applicable Patents in the Orange Book**,** including payment of all costs and expenses related to such maintenance incurred after the Effective Date. The listing and maintaining Party shall provide the other Party with its planned listings in advance of their submission with sufficient time for the other Party to review and provide comments. The listing and maintaining Party shall consider any such comments in good faith. Upon request of the listing and maintaining Party, the other Party shall cooperate in the filing of appropriate information with the FDA listing such Patents in the Orange Book.

12.6 **Infringement of Patents by Third Parties**.

(a) **Notification**. Each Party shall promptly notify the other Party in writing of any existing, alleged or threatened infringement of the Licensed [***] Patents, Licensed Product Improvement Patents, Ultragenyx [***] Patents, Option Product Patents, Option Product Improvement Patents, Ultragenyx Pipeline Patents, Ultragenyx Pipeline Improvement Patents, and Joint Patents in the Licensed Field in the Territory of which it becomes aware, and shall provide all Information in such Party's possession or control demonstrating such infringement.

(b) **Infringement Action**.

(i) Takeda shall have the first right, but not the obligation, to bring an appropriate suit or other action against any Third Party engaged in any existing, alleged or threatened infringement related to the Joint Patents, Licensed [***] Patents, Licensed Product Improvement Patents, Ultragenyx [***] Patents, Option Product Patents, and Option Product Improvement Patents, in each case where relating to Licensed Products or Research Products (a "Takeda Product Infringement"), subject to Section 12.6(b)(ii) through 12.6(b)(iv); provided that if a Takeda Product Infringement concerns the enforcement of any Valid Claim against a Third Party making, using, selling, offering for sale, or importing solely within the Ultragenyx Field, Takeda must receive Ultragenyx's prior consent with respect to all strategic decisions in connection with such Takeda Product Infringement, such consent not to be unreasonably withheld, conditioned, or delayed; and provided further that if Takeda is not Developing or Commercializing the Licensed [***] Product in the Takeda Field, then the foregoing first right with respect to a Takeda Product Infringement shall become Ultragenyx's first right hereunder. Ultragenyx shall have the first right, but not the obligation, to bring an appropriate suit or other action against any Third Party engaged in any existing, alleged or threatened infringement related to the Joint Patents, Ultragenyx Pipeline Patents and Ultragenyx Pipeline Improvement Patents, in each case where relating to an Ultragenyx Pipeline Product (an "Ultragenyx Product Infringement"), subject to Section 12.6(b)(ii) through 12.6(b)(iv). Notwithstanding the foregoing, following the execution of an Option Product License Agreement or Exercised Product License Agreement, the terms of such license agreement shall govern the handling of the infringement actions relating to the Patents covering such Licensed Option Product or Exercised Product, respectively, that is the subject of such license agreement.

(ii) The Parties shall discuss how to address each Takeda Product Infringement and Ultragenyx Product Infringement and the Party with the first right to enforce shall consider in good faith the input of the other Party in determining how to proceed. The Party with the first right to enforce shall notify the other Party of its election to take any action in accordance with Section 12.6(b)(i) within ten (10) Business Days before any time limit set forth in an Applicable Laws or regulation, including the time limits set forth under the Hatch Waxman Act. In the event such Party does not so elect, it shall so notify the other Party in writing, and the other Party shall have the right to commence a suit or take action to enforce the applicable Patent against such Third Party perpetrating such Takeda Product Infringement or Ultragenyx Product Infringement, as applicable, in the applicable portion of the Territory at its own cost and expense. If one Party elects to bring suit or take action against the Takeda Product Infringement or Ultragenyx Product Infringement, as applicable, then the other Party (at its expense) shall have the right, prior to commencement of the trial, suit or action, to join any such suit or action.

(iii) Each Party shall provide to the Party enforcing any such rights under this Section 12.6(b) reasonable assistance in such enforcement, at such enforcing Party's request and expense, including joining such action as a party plaintiff if required by Applicable Laws to pursue such action. The enforcing Party shall keep the other Party regularly informed of the status and progress of such enforcement efforts and shall reasonably consider the other Party's comments on any important aspects of such enforcement, including determination of litigation strategy and filing of important papers to the competent court.

(iv) Subject to this Section 12.6(b)(iv), the enforcing Party shall be solely responsible for all costs and expenses arising from a suit or action against a Takeda Product Infringement or Ultragenyx Product Infringement, as applicable. For the avoidance of doubt, the enforcing Party shall not be responsible for the other Party's internal costs (e.g., FTEs) incurred as a result of the other Party's cooperation with the enforcement action as provided in Section 12.6(b)(iii). The Party not bringing an action with respect to the Takeda Product Infringement or Ultragenyx Product Infringement, as applicable, under this Section 12.6(b) shall be entitled to separate representation in such matter by counsel of its own choice and at its own expense, but such Party shall at all times cooperate fully with the Party bringing such action.

(c) **Settlement**. The enforcing Party may settle any claim, suit or action that it has brought under this Section 12.6 without the prior written consent of the other Party; provided that any such settlement does not negatively impact the non-enforcing Party's rights or interests in such non-enforcing Party's territory or field.

(d) **Allocation of Proceeds**. If either Party recovers monetary damages from any Third Party in a suit or action brought under Sections 12.6(b), 12.6(c), or 12.8(b) or any royalties from a license agreement with a Third Party related to any alleged Takeda Product Infringement or Ultragenyx Product Infringement, as applicable, such recovery shall be allocated first to the reimbursement of any expenses incurred by the Parties in such suit or action, and any remaining amounts shall be split as follows: (i) if such suit or action is initiated or defended by Ultragenyx, such amounts shall be retained by Ultragenyx, or (ii) if such suit or action was initiated or defended by Takeda, such amounts shall be retained by Takeda.

12.7 **Infringement of Third Party Rights in the Territory**.

(a) **Notice**. If any Licensed Product used or sold by either Party, its Affiliates, licensees or sublicensees becomes the subject of a Third Party's claim or assertion of infringement of a Patent granted in either Party's field or territory, the Party first having notice of the claim or assertion shall promptly notify the other Party, the Parties shall agree on and enter into an "identity of interest agreement" wherein such Parties agree to their shared, mutual interest in the outcome of such potential dispute, and thereafter, the Parties shall promptly meet to consider the claim or assertion and the appropriate course of action.

(b) **Defense**.

(i) Ultragenyx shall have the first right, but not the obligation, to defend any Third Party claim or assertion of infringement of a Patent described in Section 12.7(a) above by Ultragenyx Pipeline Products, at Ultragenyx's expense. If Ultragenyx does not commence actions to defend such claim within thirty (30) days after it receives notice thereof (or within thirty (30) days after it should have given notice thereof to Takeda as required by Section 12.7(a)), then, to the extent allowed by Applicable Laws, Takeda shall have the right, but not the obligation, to control the defense of such claim by counsel of its choice, at Takeda's expense. The non-defending Party shall reasonably cooperate with the Party conducting the defense of the claim or assertion, including if required to conduct such defense, furnishing a power of attorney.

(ii) Takeda shall have the first right, but not the obligation, to defend any Third Party claim or assertion of infringement of a Patent described in Section 12.7(a) above by Licensed [***] Products, Licensed Analog Products, Candidate Products or Option Products, at Takeda's expense. If Takeda does not commence actions to defend such claim within thirty (30) days after it receives notice thereof (or within thirty (30) days after it should have given notice thereof to Ultragenyx as required by Section 12.7(a)), then, to the extent allowed by Applicable Laws, Ultragenyx shall have the right, but not the obligation, to control the defense of such claim by counsel of its choice, at Ultragenyx's expense. The non-defending Party shall reasonably cooperate with the Party conducting the defense of the claim or assertion, including if required to conduct such defense, furnishing a power of attorney.

(iii) Notwithstanding the foregoing, following the execution of an Option Product License Agreement or Exercised Product License Agreement, the terms of such license agreement shall govern the handling of the defense against infringement by Product(s) that are the subject of the applicable license agreement.

(c) **Settlement; Licenses**. Neither Party shall enter into any settlement of any claim described in this Section 12.7 that negatively affects the other Party's rights or interests without such other Party's written consent, which consent shall not be unreasonably withheld, conditioned or delayed. Each Party shall have the right to decline to defend or to tender defense of any such claim to the other Party upon reasonable notice, including if the other Party fails to agree to a settlement that such Party proposes. In the event that it is determined by any court of competent jurisdiction that the Exploitation of a Product in the Licensed Field in the Ultragenyx Territory, conducted in accordance with the terms and conditions of this Agreement, infringes, or the JSC determines that such activities are likely to infringe, any patent, copyright, trademark, data exclusivity right or trade secret right arising under Applicable Laws of any Third Party, Ultragenyx shall use Commercially Reasonable Efforts to: (i) procure a license from such Third Party authorizing Ultragenyx to continue to conduct such activities; or (ii) modify such activities so as to render it non-infringing.

12.8 **Patent Oppositions and Other Proceedings**.

(a) **Third-Party Patent Rights**. If either Party desires to bring an opposition, action for declaratory judgment, nullity action, interference, declaration for non-infringement, reexamination or other attack upon the validity, title or enforceability of a Patent owned or controlled by a Third Party and having one or more claims that covers a Product, or the use, sale, offer for sale or importation of a Product (except insofar as such action is a counterclaim to or defense of, or accompanies a defense of, a Third Party's claim or assertion of infringement under Section 12.7, in which case the provisions of Section 12.7 shall govern), such Party shall so notify the other Party and the Parties shall promptly confer to determine whether to bring such action or the manner in which to settle such action. Ultragenyx shall have the exclusive right, but not the obligation, to bring at its own expense and in its sole control such action in the Territory with respect to Ultragenyx Pipeline Products. Takeda shall have the exclusive right, but not the obligation, to bring at its own expense and in its sole control such action with respect to Licensed [***] Products, Licensed Analog Products and Research Products in the Territory. If the

Party with the first right does not bring such an action, within ninety (90) days of notification thereof pursuant to this Section 12.8(a) (or earlier, if required by the nature of the proceeding), then the other Party shall have the right, but not the obligation, to bring, at its sole expense, such action. The Party not bringing an action under this Section 12.8(a) shall be entitled to separate representation in such proceeding by counsel of its own choice and at its own expense, and shall cooperate fully with the Party bringing such action. Any awards or amounts received in bringing any such action shall be first allocated to reimburse the initiating Party's expenses in such action and any remaining amounts shall be retained by such Party.

(b) **Parties' Patent Rights**. If any Licensed [***] Patents, Licensed Product Improvement Patent, Ultragenyx [***] Patents, Option Product Patent, Option Product Improvement Patent, Ultragenyx Pipeline Patent, Ultragenyx Pipeline Improvement Patent, or Joint Patent becomes the subject of any proceeding commenced by a Third Party within the Territory in connection with an opposition, reexamination request, action for declaratory judgment, nullity action, interference or other attack upon the validity, title or enforceability thereof (except insofar as such action is a counterclaim to or defense of, or accompanies a defense of, an action for infringement against a Third Party under Section 12.6, in which case the provisions of Section 12.6 shall govern), then the Party responsible for filing, preparing, prosecuting and maintaining such Patent as set forth in Section 12.3, shall control such defense at its own cost and expense. The controlling Party shall permit the non-controlling Party to participate in the proceeding to the extent permissible under Applicable Laws, and to be represented by its own counsel in such proceeding, at the non-controlling Party's expense. If the controlling Party decides that it does not wish to defend against such action, then the other Party shall have a backup right to assume defense of such Third-Party action at its own expense. Any awards or amounts received in defending any such Third-Party action shall be allocated between the Parties as provided in Section 12.6(d).

ARTICLE 13 – REPRESENTATIONS AND WARRANTIES

13.1 **Mutual Representations, Warranties and Covenants**. Each of the Parties hereby represents and warrants to the other Party as of the Execution Date and covenants that:

(a) **Organization.** It is a corporation duly organized, validly existing, and in good standing under the laws of the jurisdiction of its organization, and has all requisite power and authority, corporate or otherwise, to execute, deliver, and perform this Agreement.

(b) **Binding Agreement.** This Agreement is a legal and valid obligation binding upon such Party and enforceable in accordance with its terms, subject to the effects of bankruptcy, insolvency, or other laws of general application affecting the enforcement of creditor rights, judicial principles affecting the availability of specific performance, and general principles of equity (whether enforceability is considered a proceeding at law or equity).

(c) **Authorization.** The execution, delivery, and performance of this Agreement by such Party have been duly authorized by all necessary corporate action and do not conflict with any agreement, instrument, or understanding, oral or written, to which it is a party or by which it is bound, nor violate any Applicable Laws or any order, writ, judgment, injunction, decree,

determination, or award of any court or governmental body, or administrative or other agency presently in effect applicable to such Party.

(d) **No Further Approval.** Subject to Section 18.1, it is not aware of any government authorization, consent, approval, license, exemption of or filing or registration with any court or governmental department, commission, board, bureau, agency or instrumentality, domestic or foreign, under any Applicable Laws, currently in effect, necessary for, or in connection with, the transactions contemplated by this Agreement or any other agreement or instrument executed in connection herewith, or for the performance by it of its obligations under this Agreement and such other agreements (save for Regulatory Approvals and similar authorizations from Regulatory Authorities necessary for the Exploitation of the Compounds and the Products as contemplated hereunder).

(e) **No Inconsistent Obligations.** Neither Party is under any obligation, contractual or otherwise, to any Person that conflicts with or is inconsistent in any material respect with the terms of this Agreement, or that would impede the diligent and complete fulfillment of its obligations hereunder.

(f) **Transparency Reporting**. Each Party shall be responsible for tracking and reporting transfers of value initiated and controlled by its and its Affiliates' employees, independent contractors, and agents pursuant to the requirements of the marketing reporting laws of any Government Authority in the Territory, including Section 6002 of the Patient Protection and Affordable Care Act, commonly referred to as the "Sunshine Act."

(g) Neither Party nor any of its Affiliates has been debarred by the FDA, is subject to any similar sanction of other Regulatory Authorities in the Territory, and neither Party nor any of its Affiliates has used, or will engage, in any capacity, in connection with this Agreement or any ancillary agreements (if any), any Person who either has been debarred by such a Regulatory Authority, or is the subject of a conviction described in Section 306 of the FFDCA. Each Party shall inform the other in writing promptly if it or any Person engaged by such Party or any of its Affiliates who is performing services under this Agreement or any ancillary agreements (if any) is debarred or is the subject of a conviction described in Section 306 of the FFDCA, or if any action, suit, claim, investigation or legal or administrative proceeding is pending or, to such Party's Knowledge, is threatened, relating to the debarment or conviction of such Party, any of its Affiliates or any such Person performing services hereunder or thereunder.

13.2 **Additional Representations, Warranties and Covenants of Takeda**. Takeda represents and warrants as of the Execution Date and covenants to Ultragenyx that:

(a) Takeda has all rights necessary to grant the options and licenses under the Licensed [***] Technology and Option Product Technology and rights of cross-reference under Regulatory Materials, in each case, existing as of the Execution Date that it grants to Ultragenyx in this Agreement. For the duration of the Term, Takeda shall not, and shall cause its Affiliates not to, grant to any Third Party rights in the Licensed Field or the Ultragenyx Field, as applicable, in the Territory that encumber, diminish or conflict with the rights granted to

Ultragenyx hereunder with respect to the Licensed [***] Technology, Option Product Technology, Joint Intellectual Property or Regulatory Materials.

(b) (i) The Patents set forth in Exhibit 1.168 represent all Takeda Patents, (ii) to Takeda's Knowledge, the Compounds set forth in Exhibit 13.2(b) represent all structures Controlled by Takeda that are [***], and (i) to Takeda's Knowledge, the Compound set forth in Exhibit 1.94 represents the sole Licensed [***] Compound. Takeda (Y) is the sole and exclusive owner of the entire right, title and interest in the Takeda Patents, and (Z) to Takeda's Knowledge, the sole and exclusive owner of the entire right, title and interest in the Licensed [***] Compound and Licensed Analog Compounds, and in each of cases (Y) and (Z), free of any encumbrance, lien, or claim of ownership by any Third Party.

(c) To Takeda's Knowledge, there is no actual or threatened infringement or misappropriation of the Licensed [***] Technology and Option Product Technology by any Person in the Territory.

(d) The Takeda Patents are being diligently prosecuted in the Territory in accordance with Applicable Laws. To Takeda's Knowledge, the Takeda Patents have been filed and maintained properly and correctly and all applicable fees have been paid on or before the due date for payment.

(e) To Takeda's Knowledge, each of the Takeda Patents properly identifies each and every inventor of the claims thereof as determined in accordance with Applicable Laws of the jurisdiction in which such Takeda Patent is issued or such application is pending.

(f) To the extent permissible under Applicable Laws, all employees of Takeda or its Affiliates performing activities under this Agreement are and shall be under an obligation to assign all right, title and interest in and to their Inventions and intellectual property rights therein, to Takeda or its Affiliate(s) as the sole owner thereof. Ultragenyx shall have no obligation to contribute to any remuneration of any inventor employed or previously employed by Takeda or any of its Affiliates in respect of any such Inventions and intellectual property rights therein that are so assigned to Takeda or its Affiliate(s). Takeda will pay all such remuneration due to such inventors with respect to such Inventions and intellectual property rights therein.

(g) The Inventions claimed or disclosed by the Takeda Patents (i) were not conceived, discovered, developed, or otherwise made in connection with any research activities funded, in whole or in part, by the federal government of the U.S. or any agency thereof, (ii) are not a "subject invention" as that term is described in 35 U.S.C. Section 201(f), and (iii) are not otherwise subject to the provisions of the Bayh-Dole Act.

(h) To Takeda's Knowledge, there are no material claims, judgments, or settlements against, or amounts with respect thereto, owed by Takeda or any of its Affiliates to any Third Parties relating to the Regulatory Materials, Licensed [***] Technology or Option Product Technology in the Territory.

(i) No claim or litigation in the Territory has been brought or, to Takeda's Knowledge, threatened by any Person alleging, and Takeda has no Knowledge of any claim, whether or not asserted: (i) that any of the Takeda Patents is invalid or unenforceable, (ii) that the Regulatory Materials, or the disclosing, copying, making, assigning, or licensing of the Regulatory Materials, violates, infringes, or otherwise conflicts or interferes with, or would violate, infringe, or otherwise conflict or interfere with, any intellectual property or proprietary right of any Person; or (iii) related to the Development or Commercialization of the Licensed Products or Research Products, including any claims of Product Liability.

(j) Takeda has no Knowledge of any material adverse information with respect to the safety and efficacy of any Licensed Product or Research Product that has not been disclosed to Ultragenyx, and all such information that has been disclosed is true, correct, and complete in all material respects.

(k) To Takeda's Knowledge, Takeda and its Affiliates have generated, prepared, maintained, and retained all material Regulatory Materials in the Licensed Field that are required to be maintained or retained pursuant to and in accordance with GCP, GLP and other Applicable Laws, and all such information is true, complete and correct in all material respects and what it purports to be.

(l) Takeda**,** without the prior written consent of Ultragenyx, during the Term, will not solicit, induce, encourage, or participate in soliciting, inducing, or encouraging any employee of Ultragenyx, or any of its Affiliates, to terminate his or her relationship with Ultragenyx or Ultragenyx's Affiliate. An offer of employment to an employee of Ultragenyx by Takeda which results directly from unsolicited responses to general advertisements for employment will not be deemed to be in violation of this provision.

(m) In performing its obligations under this Agreement, Takeda shall, and shall cause its Affiliates to, comply with all Applicable Laws, including any applicable anti-corruption or anti-bribery laws or regulation, of any Governmental Authority with jurisdiction over the activities performed by Takeda or its Affiliates in furtherance of such obligations.

13.3 **Additional Representations, Warranties and Covenants of Ultragenyx**. Ultragenyx represents and warrants as of the Execution Date and covenants to Takeda that:

(a) Ultragenyx and its Affiliates have provided or made available to Takeda prior to the Execution Date, true, complete, and correct copies (as of the Execution Date) of all Ultragenyx In-License Agreements.

(b) Ultragenyx has all rights applicable necessary to grant the options and licenses under the Ultragenyx Intellectual Property and rights of cross-reference under Regulatory Materials, in each case, that it grants to Takeda in this Agreement. For the duration of the Term, Ultragenyx shall not, and shall cause its Affiliates not to, grant to any Third Party rights in the Takeda Field in the Territory or the Licensed Field in the Takeda Territory, as applicable, that encumber, diminish or conflict with the rights granted to Takeda hereunder with respect to the Ultragenyx Intellectual Property, Joint Intellectual Property or Regulatory Materials.

(c) The Patents set forth in Exhibit 1.188 represent all Ultragenyx Patents. Ultragenyx is the sole and exclusive owner of the entire right, title and interest in the Ultragenyx Patents free of any encumbrance, lien, or claim of ownership by any Third Party.

(d) To Ultragenyx's Knowledge, there is no actual or threatened infringement or misappropriation of the Ultragenyx Intellectual Property by any Person in the Territory.

(e) The Ultragenyx Patents are being diligently prosecuted in the Territory in accordance with Applicable Laws and consistent with Ultragenyx's current prosecution practices. To Ultragenyx's Knowledge, the Ultragenyx Patents have been filed and maintained properly and correctly and all applicable fees have been paid on or before the due date for payment.

(f) To Ultragenyx's Knowledge, each of the Ultragenyx Patents properly identifies each and every inventor of the claims thereof as determined in accordance with Applicable Laws of the jurisdiction in which such Ultragenyx Patent is issued or such application is pending.

(g) To the extent permissible under Applicable Laws, all employees of Ultragenyx or its Affiliates performing activities under this Agreement shall be under an obligation to assign all right, title and interest in and to their Inventions, and intellectual property rights therein, to Ultragenyx or its Affiliate(s) as the sole owner thereof. Takeda shall have no obligation to contribute to any remuneration of any inventor employed or previously employed by Ultragenyx or any of its Affiliates in respect of any such inventions, Information and discoveries and intellectual property rights therein that are so assigned to Ultragenyx or its Affiliate(s). Ultragenyx will pay all such remuneration due to such inventors with respect to such Inventions and intellectual property rights therein.

(h) To Ultragenyx's Knowledge, the Inventions claimed or disclosed by the Ultragenyx Patents (i) were not conceived, discovered, developed, or otherwise made in connection with any research activities funded, in whole or in part, by the federal government of the U.S. or any agency thereof, (ii) are not a "subject invention" as that term is described in 35 U.S.C. Section 201(f), and (iii) are not otherwise subject to the provisions of the Bayh-Dole Act.

(i) To Ultragenyx's Knowledge, there are no material claims, judgments, or settlements against, or amounts with respect thereto, owed by Ultragenyx or any of its Affiliates to any Third Parties relating to the Regulatory Materials or the Ultragenyx Intellectual Property in the Territory.

(j) Ultragenyx has no Knowledge of any material adverse information with respect to the safety and efficacy of any Compound or Product that has not been disclosed to Takeda, and all such information that has been disclosed is true, correct, and complete in all material respects.

(k) No claim or litigation in the Territory has been brought or, to Ultragenyx's Knowledge, threatened by any Person alleging, and Ultragenyx has no Knowledge of any claim, whether or not asserted: (i) that any of the Ultragenyx Patents is invalid or unenforceable, (ii) that the Regulatory Materials, the Ultragenyx Intellectual Property, or the disclosing, copying,

making, assigning, or licensing of the Regulatory Materials or the Ultragenyx Intellectual Property, violates, infringes, or otherwise conflicts or interferes with, or would violate, infringe, or otherwise conflict or interfere with, any intellectual property or proprietary right of any Person; or (iii) related to the Development or Commercialization of the Products, including any claims of Product Liability.

(l) In performing its obligations under this Agreement Ultragenyx shall, and shall cause its Affiliates to, comply with all Applicable Laws, including any applicable anti-corruption or anti-bribery laws or regulation, of any Governmental Authority with jurisdiction over the activities performed by Ultragenyx or its Affiliates in furtherance of such obligations.

(m) Ultragenyx**,** without the prior written consent of Takeda, during the Term, will not solicit, induce, encourage, or participate in soliciting, inducing, or encouraging any employee of Takeda, or any of its Affiliates, to terminate his or her relationship with Takeda or Takeda's Affiliate. An offer of employment to an employee of Takeda by Ultragenyx which results directly from unsolicited responses to general advertisements for employment will not be deemed to be in violation of this provision.

(n) [***].

(o) Ultragenyx has provided Takeda with true and correct copies (as of the Execution Date) of all Ultragenyx In-License Agreements in effect as of the Execution Date. None of Ultragenyx, its Affiliates and, to their Knowledge, any Third Party, is in breach of any Ultragenyx In-License Agreement and none of Ultragenyx, its Affiliates and, to their Knowledge, any other party to any Ultragenyx In-License Agreement has threatened to terminate, or has otherwise alleged any material breach under, such agreement and each Ultragenyx In-License Agreement is in full force and effect in accordance with its terms

13.4 **No Other Representations or Warranties**. EXCEPT AS EXPRESSLY SET FORTH IN THIS ARTICLE 13, THE PARTIES MAKE NO REPRESENTATIONS OR WARRANTIES OF ANY KIND WHATSOEVER, EITHER EXPRESS OR IMPLIED, WRITTEN OR ORAL, EITHER IN FACT OR BY OPERATION OF LAW, BY STATUTE OR OTHERWISE, AND EACH PARTY SPECIFICALLY DISCLAIMS ANY OTHER WARRANTIES, INCLUDING ANY EXPRESS OR IMPLIED WARRANTY OF QUALITY, MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, OR WARRANTY OF NON-INFRINGEMENT OR AS TO THE VALIDITY OF ANY PATENTS IN THE TERRITORY.

ARTICLE 14 – CONFIDENTIALITY

14.1 **Nondisclosure.** Each Party agrees that, during the Term and for a period of ten (10) years thereafter, a Party (the "Receiving Party") receiving Confidential Information of the other Party (the "Disclosing Party") shall (a) maintain in confidence such Confidential Information using not less than the efforts such Receiving Party uses to maintain in confidence its own confidential or proprietary Information of similar kind and value, (b) not disclose such

Confidential Information to any Third Party without the prior written consent of the Disclosing Party, except for disclosures expressly permitted below, and (c) not use such Confidential Information for any purpose except those permitted by this Agreement (it being understood that this Section 14.1 shall not create or imply any rights or licenses not expressly granted under this Agreement). Notwithstanding anything to the contrary in the foregoing, the obligations of confidentiality and non-use with respect to any trade secret within such Confidential Information shall survive such ten (10) year period for so long as such Confidential Information remains protected as a trade secret under Applicable Laws.

14.2 **Exceptions.** The obligations in Section 14.1 shall not apply with respect to any portion of the Confidential Information that the Receiving Party can show by competent evidence:

(a) is publicly disclosed by the Disclosing Party, either before or after it is disclosed to the Receiving Party hereunder;

(b) is known to the Receiving Party or any of its Affiliates, without any obligation to keep it confidential or any restriction on its use, prior to disclosure by the Disclosing Party;

(c) is subsequently disclosed to the Receiving Party or any of its Affiliates on a non- confidential basis by a Third Party that, to the Receiving Party's Knowledge, is not bound by a similar duty of confidentiality or restriction on its use;

(d) is now, or hereafter becomes, through no act or failure to act on the part of the Receiving Party or any of its Affiliates, generally known or available, either before or after it is disclosed to the Receiving Party;

(e) is independently discovered or developed by or on behalf of the Receiving Party or any of its Affiliates without the use of or access to Confidential Information belonging to the Disclosing Party; or

(f) is the subject of written permission to disclose provided by the Disclosing Party.

14.3 **Authorized Disclosure.** The Receiving Party may disclose Confidential Information belonging to the Disclosing Party only to the extent such disclosure is reasonably necessary in the following instances: filing or prosecuting Patents as permitted by this Agreement;

(b) filing Regulatory Materials in order to obtain or maintain Regulatory Approvals;

(c) prosecuting or defending litigation, including responding to a subpoena in a Third Party litigation;

(d) complying with Applicable Laws or regulations or court or administrative orders;
or

(e) to its Affiliates, sublicensees or prospective sublicensees, subcontractors or prospective subcontractors, payors, consultants, agents and advisors on a "need-to-know" basis

in order for the Receiving Party to exercise its rights or fulfill its obligations under this Agreement, each of whom prior to disclosure must be bound by obligations of confidentiality and restrictions on use of such Confidential Information that are no less restrictive than those set forth in this ARTICLE 14; provided, however, that, in each of the above situations, the Receiving Party shall remain responsible for any failure by any Person who receives Confidential Information pursuant to this Section 14.3 to treat such Confidential Information as required under this ARTICLE 14.

(f) If and whenever any Confidential Information is disclosed in accordance with this Section 14.3, such disclosure shall not cause any such information to cease to be Confidential Information except to the extent that such disclosure results in a public disclosure of such information (other than by breach of this Agreement). Notwithstanding the foregoing, in the event a Party is required to make a disclosure of the other Party's Confidential Information pursuant to clauses (a) through (d) of this Section 14.3, it will, except where impracticable, give reasonable advance notice to the other Party of such disclosure and use not less than the same efforts to secure confidential treatment of such information as it would to protect its own confidential information from disclosure and shall be jointly and severally liable for any breach of this ARTICLE 14 by such Person.

14.4 **Terms of this Agreement.** The Parties acknowledge that this Agreement and all of the respective terms of this Agreement shall be treated as Confidential Information of both Parties.

14.5 **Publicity.** The Parties shall make a joint public announcement of the execution of this Agreement in the form attached as Exhibit 14.5, which shall be issued at a time to be mutually agreed by the Parties. Each Party agrees not to issue any other press release or other public statement disclosing other information relating to this Agreement or the transactions contemplated hereby that contains information not previously publicly disclosed in accordance with this Section 14.5 without the prior written consent of the other Party, not to be unreasonably withheld, conditioned or delayed.

14.6 **Securities Filings.** Notwithstanding anything to the contrary in this ARTICLE 14, in the event either Party proposes to file with the Securities and Exchange Commission or the securities regulators of any state or other jurisdiction a registration statement or any other disclosure document that describes or refers to the terms and conditions of this Agreement or any related agreements between the Parties, such Party shall notify the other Party of such intention and shall provide the other Party with a copy of relevant portions of the proposed filing at least ten (10) Business Days prior to such filing (and any revisions to such portions of the proposed filing a reasonable time prior to the filing thereof), including any exhibits thereto that refer to the other Party or the terms and conditions of this Agreement or any related agreements between the Parties. The Party making such filing shall cooperate in good faith with the other Party to obtain confidential treatment of the terms and conditions of this Agreement or any related agreements between the Parties that the other Party requests to be kept confidential or otherwise afforded confidential treatment, and shall only disclose Confidential Information that it is reasonably advised by outside counsel is legally required to be disclosed. No such notice and provision of a copy shall be required if the description of or reference to this Agreement or a related agreement

between the Parties contained in the proposed filing has been included in any previous filing made by the either Party in accordance with this Section 14.6 or otherwise approved by the other Party.

14.7 **Relationship to Confidentiality Agreement.** As of the Effective Date, this Agreement supersedes the Confidentiality Agreement; provided however, that all "Confidential Information" disclosed or received by the Parties thereunder shall be deemed Confidential Information hereunder and shall be subject to the terms and conditions of this Agreement.

14.8 **Equitable Relief.** Given the nature of the Confidential Information and the competitive damage that could result to a Party upon unauthorized disclosure, use or transfer of its Confidential Information to any Third Party, the Parties agree that monetary damages may not be a sufficient remedy for any breach of this ARTICLE 14. In addition to all other remedies, a Party shall be entitled to seek specific performance and injunctive and other equitable relief as a remedy for any breach or threatened breach of this ARTICLE 14.

14.9 **Publications.** All publications relating to the use of the Compound and/or a Product in the Licensed Field shall be prepared, presented and/or published in accordance with pharmaceutical industry accepted guidelines including: (a) International Committee of Medical Journal Editors (ICMJE) guidelines, (b) Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication, (c) Pharmaceutical Research and Manufacturers of America (PhRMA) guidelines, and (d) Principles on Conduct of Clinical Trials. Each Party will have the right to publish summaries of results of all Clinical Trials conducted by such Party with respect to the use of a Product in the Licensed Field after the Effective Date; *provided*, *however,* that the other Party will have the right to review and comment on all proposed publications prior to submission of such publication. The publishing Party shall provide the other Party at least sixty (60) days prior notice to review and comment on the Clinical Trials results, or non-clinical study results to be published for the purposes of preparing any necessary Patent filings.

14.10 **Clinical Trial Transparency**. Both Parties agree to collaborate to maintain compliance with all Applicable Laws related to clinical trial transparency, as well as any industry guidelines/codes of conduct, or other obligations that may apply to either the sponsor of any clinical trial and/or the owner of any Regulatory Approval, all as relates to any Research Product or Licensed Product. The Parties shall cooperate to maintain clinical trial transparency consistent with each sponsor's clinical trial registration, summary result, and data sharing transparency policies and will support disclosure of Information as needed based on the needs of the sponsors of the study or the Regulatory Approval holder with respect to any Research Product or Licensed Product.

ARTICLE 15 – TERM AND TERMINATION

15.1 **Term**. This Agreement shall become effective as of the Effective Date and shall continue in full force and effect, unless earlier terminated pursuant to this ARTICLE 15, until the later of the (a) expiration of the Collaboration Term, (b) the expiration of the Takeda Option Term, (c) the expiration of the Licensed Product Royalty Term with respect to all Licensed

Products in the Territory, or (d) the expiration of the Takeda Royalty Term with respect to all Products the Takeda Territory (the "Term").

15.2 **Termination for Material Breach**.

(a) Either Party (the "Non-breaching Party") may terminate this Agreement in its entirety (except as otherwise provided in this Section 15.2(a)) if the other Party (the "Breaching Party") has materially breached this Agreement, and such material breach has not been cured within sixty (60) days after receipt of written notice of such breach by the Breaching Party from the Non-Breaching Party (the "Cure Period"); provided, however, that, notwithstanding the foregoing, termination pursuant to this Section 15.2(a) shall be on a Compound-by-Compound and Product-by-Product basis unless such material breach materially diminishes, or materially frustrates, the value of this Agreement to the Non-breaching Party, taken as a whole, in which case the Non-breaching Party may terminate this Agreement in its entirety. Any termination of this Agreement with respect to a Compound or Product, or in its entirety, pursuant to this Section 15.2(a) shall become effective at the end of the Cure Period, unless the Breaching Party has cured any such material breach prior to the expiration of such Cure Period. The right of either Party to terminate this Agreement with respect to a Compound or Product, or in its entirety, as provided in this Section 15.2(a) shall not be affected in any way by such Party's waiver of or failure to take action with respect to any previous breach under this Agreement.

(b) If the Parties reasonably and in good faith disagree as to whether there has been a material breach, including whether such breach was material, the Party that disputes whether there has been a material breach may contest the allegation in accordance with ARTICLE 16. Notwithstanding anything to the contrary contained in Section 15.2(a), the Cure Period for any Dispute will run from the date that written notice was first provided to the Breaching Party by the Non-Breaching Party through the resolution of such Dispute pursuant to ARTICLE 16, and it is understood and acknowledged that, during the pendency of a Dispute pursuant to this Section 15.2(b), all of the terms and conditions of this Agreement shall remain in effect, and the Parties shall continue to perform all of their respective obligations under this Agreement.

(c) Notwithstanding the foregoing, following the execution of an Option Product License Agreement or Exercised Product License Agreement, the terms of such license agreement shall govern the handling of termination for material breach with respect to the activities that are the subject of such license agreement (which shall be on the basis of this Section 15.2) and any termination of this Agreement shall not affect the existence of such Option Product License Agreement or Exercised Product License Agreement.

15.3 **Termination for Safety Reasons.**

(a) Each Party shall have the right to terminate this Agreement on a Compound-by- Compound and Product-by-Product basis with respect to such Party's field and territory at any time upon providing ninety (90) days prior written notice to the other Party (i) if senior executives responsible for the terminating Party's pharmacovigilance and clinical science functions determine in good faith that the risk/benefit profile of the Compound or Product is such that the Compound or Product cannot continue to be Developed or administered to patients

safely; or (b) upon the occurrence of serious adverse events related to the use of the Compound or Product that cause the terminating Party to conclude that the continued use of the Compound or Product by patients will result in patients being exposed to a product in which the risks outweigh the benefits.

(b) Notwithstanding the foregoing, following the execution of an Option Product License Agreement or Exercised Product License Agreement, the terms of such license agreement shall govern the handling of termination for safety reasons with respect to the activities that are the subject of such license agreement (which shall be on the basis of this Section 15.3) and any termination of this Agreement shall not affect the existence of such Option Product License Agreement or Exercised Product License Agreement.

15.4 **Termination for Convenience**.

(a) Takeda shall have the right to terminate this Agreement with respect to the Takeda Option for any or no reason upon ninety (90) days written notice.

(b) Provided that Ultragenyx has completed Development activities for a Licensed [***] Product in the Takeda Field as set forth in the Initial [***] Development Plan pursuant to Section 4.3(a), after the end of the Collaboration Term Ultragenyx shall have the right to terminate this Agreement with respect to any or all Licensed Products in any or all countries for which it has rights with respect to such Licensed Products for any or no reason upon ninety (90) days written notice.

(c) Notwithstanding the foregoing, following the execution of an Option Product License Agreement or Exercised Product License Agreement, the terms of such license agreement shall govern the handling of termination for convenience with respect to the activities that are the subject of such license agreement (which shall be on the basis of this Section 15.4) and any termination of this Agreement shall not affect the existence of such Option Product License Agreement or Exercised Product License Agreement.

15.5 **Termination for Patent Challenge**.

(a) Takeda may terminate this Agreement with respect to the Licensed Products at any time upon providing written notice to Ultragenyx, if Ultragenyx, or any of Ultragenyx's Affiliates, directly, or indirectly through assistance granted to a Third Party, commences any interference or opposition proceeding, challenges the validity or enforceability of, or opposes any extension of or the grant of a supplementary protection certificate with respect to any Takeda Patent or any other Patent owned or controlled by Takeda that claims or discloses the composition of matter or the method of making or using a Licensed Product.

(b) Takeda may terminate this Agreement with respect to all Candidate Products and/or Option Products at any time upon providing written notice to Ultragenyx, if Ultragenyx, or any of Ultragenyx's Affiliates, directly, or indirectly through assistance granted to a Third Party, commences any interference or opposition proceeding, challenges the validity or enforceability of, or opposes any extension of or the grant of a supplementary protection

certificate with respect to any Takeda Patent or any other Patent Controlled by Takeda that claims or discloses the composition of matter or the method of making or using a Candidate Product and/or Option Product.

(c) Ultragenyx may terminate this Agreement with respect to an Ultragenyx Pipeline Product at any time upon providing written notice to Takeda, if Takeda, or any of Takeda's Affiliates, directly, or indirectly through assistance granted to a Third Party, commences any interference or opposition proceeding, challenges the validity or enforceability of, or opposes any extension of or the grant of a supplementary protection certificate with respect to any Ultragenyx Patent or any other Patent Controlled by Ultragenyx that claims or discloses the composition of matter or the method of making or using such Ultragenyx Pipeline Product.

(d) Notwithstanding the foregoing, following the execution of an Option Product License Agreement or Exercised Product License Agreement, the terms of such license agreement shall govern the handling of termination for patent challenge with respect to the activities that are the subject of such license agreement (which shall be on the basis of this Section 15.5) and any termination of this Agreement shall not affect the existence of such Option Product License Agreement or Exercised Product License Agreement.

15.6 **Termination for Insolvency**.

(a) Either Party may terminate this Agreement in its entirety upon providing written notice to the other Party on or after the time that such other Party makes a general assignment for the benefit of creditors, files an insolvency petition in bankruptcy, petitions for or acquiesces in the appointment of any receiver, trustee or similar officer to liquidate or conserve its business or any substantial part of its assets, commences under the laws of any jurisdiction any proceeding involving its insolvency, bankruptcy, reorganization, adjustment of debt, dissolution, liquidation or any other similar proceeding for the release of financially distressed debtors, or becomes a party to any proceeding or action of the type described above, and such proceeding or action remains un-dismissed or un-stayed for a period of more than ninety (90) days.

(b) All rights and licenses granted under or pursuant to this Agreement are, and shall otherwise be deemed to be, for purposes of Section 365(n) of Title 11 of the United States Code and other similar laws in any other jurisdiction outside of the Territory (collectively, the "Bankruptcy Laws"), licenses of rights to "intellectual property" as defined under the Bankruptcy Laws. If a case is commenced during the Term by or against a Party under Bankruptcy Laws then, unless and until this Agreement is rejected as provided pursuant to such Bankruptcy Laws, such Party (in any capacity, including debtor-in-possession) and its successors and assigns (including a Title 11 trustee) shall perform all of the obligations in this Agreement intended to be performed by such Party. If a case is commenced during the Term by or against a Party under the Bankruptcy Laws, this Agreement is rejected as provided for under the Bankruptcy Laws, and the non-bankrupt Party elects to retain its rights hereunder as provided for under the Bankruptcy Laws, then the Party subject to such case under the Bankruptcy Laws (in any capacity, including debtor-in-possession) and its successors and assigns (including a Title 11 trustee), shall provide to the non-bankrupt Party copies of all Patents and Information necessary for the non-bankrupt Party to prosecute, maintain and enjoy its rights under the terms of this

Agreement. All rights, powers and remedies of the non-bankrupt Party as provided herein are in addition to and not in substitution for any and all other rights, powers and remedies now or hereafter existing at law or in equity (including the Bankruptcy Laws) in the event of the commencement of a case by or against a Party under the Bankruptcy Laws. In particular, it is the intention and understanding of the Parties to this Agreement that the rights granted to the Parties under this Section 15.6 are essential to the Parties' respective businesses and the Parties acknowledge that damages are not an adequate remedy.

(c) Notwithstanding the foregoing, following the execution of an Option Product License Agreement or Exercised Product License Agreement, the terms of such license agreement shall govern the handling of termination for insolvency with respect to the activities that are the subject of such license agreement (which shall be on the basis of this Section 15.6) and any termination of this Agreement shall not affect the existence of such Option Product License Agreement or Exercised Product License Agreement.

15.7 **Effects of Termination**.

(a) **Effects of Termination of Agreement in its Entirety**

(i) In the event of a termination of this Agreement in its entirety by Ultragenyx pursuant to Section 15.2 (Breach) and 15.6 (Insolvency), Ultragenyx may elect either of the following options (A) or (B) by providing written notice of its election with its notice of termination:

(A) to effectuate actual termination of this Agreement in its entirety, in which case the following shall apply:

(I) all rights and licenses granted to Ultragenyx hereunder shall terminate immediately;

(II) all rights and licenses granted by Ultragenyx hereunder shall terminate immediately other than the Takeda [***] License, which license shall become non-exclusive under any intellectual property not assigned to Takeda pursuant to the remainder of this Section 15.7(a)(i)(A), and which license shall apply to the Licensed [***] Compound, Licensed Analog Compounds, Licensed Products and Research Products;

(III) Ultragenyx, as soon as reasonably practical after the effective date of such termination, shall provide to Takeda, as applicable and to the extent permitted under any applicable Third Party contract, (1) any Information, including copies of all Clinical Trial data and results, and the like developed by or for the benefit of Ultragenyx relating to a Licensed Product or Research Product, and (2) other documents to the extent relating to the Licensed [***] Compounds, Licensed Analog Compounds, [***] Compounds, Candidate Products, Licensed Products or Research Products that are necessary for their Exploitation. Ultragenyx will cooperate with Takeda to provide a transfer of such Information and documents at Takeda's expense. At Takeda's request, Ultragenyx shall assign to Takeda any and all agreements to which Ultragenyx, or its Affiliate, and a Third Party are parties, and that govern the Exploitation

activities conducted in connection with such Compounds or Products prior to such termination, or, if such assignment is not permitted under the relevant agreement: (i) grant to Takeda other rights to provide to Takeda the benefit of such non-assignable agreement, at Takeda's expense, to the extent permitted under the terms of such non-assignable agreement; or (ii) to the extent not permitted under the terms of such non-assignable agreement, the Parties shall discuss in good faith an alternative solution to enable Takeda to receive, at Takeda's expense, the benefit of the terms of such non-assignable agreement. In addition to the actions contemplated in this Section 15.7(a)(i)(A)(III), Ultragenyx shall take such other actions and execute such other instruments, assignments and documents, at Takeda's expense, as may be necessary to effect the transfer of rights to such Compound(s) and Product(s) hereunder to Takeda;

(IV) Ultragenyx shall, at Takeda's expense, transfer to Takeda any and all Regulatory Documentation related to a Licensed Product or Research Product, including any Product INDs and Product Regulatory Approvals and, upon Takeda's request, shall make available to Takeda any other relevant information reasonably related to such Regulatory Documentation; and

(V) effective on the date of termination, Ultragenyx, for itself and on behalf of its Affiliates, hereby assigns (and to the extent such assignment can only be made in the future hereby agrees to assign) to Takeda all right, title and interest in and to any Licensed Product Improvements, Licensed Product Improvement Patents, Option Product Improvements, and Option Product Improvement Patents, in each case where Controlled by Ultragenyx or its Affiliates. Ultragenyx will, at Takeda's expense, execute and record assignments and other necessary documents consistent with such change in ownership; or

(B) in lieu of actual termination under (A) above, Ultragenyx may elect that all rights and licenses granted to Ultragenyx hereunder shall continue under this Agreement and any milestone or royalty payments that become due to Takeda by Ultragenyx with respect to Licensed Product after such termination shall be [***] and paid to Takeda in accordance with the payment provisions of this Agreement. This Section 15.7(a)(i)(B) may only be exercised once.

(ii) In the event of a termination of this Agreement in its entirety by Takeda pursuant to Section 15.2 (Breach) or 15.6 (Insolvency), Takeda may elect either of the following options (A) or (B) by providing written notice of its election with its notice of termination:

(A) to effectuate actual termination of this Agreement in its entirety, in which case the following shall apply:

(I) all rights and licenses granted to Takeda hereunder shall terminate immediately, other than the Takeda [***] License, which license shall become non-exclusive under any intellectual property not assigned to Takeda pursuant to the remainder of this Section 15.7(a)(ii)(A), and which licenses shall apply to the Licensed [***] Compound, Licensed Analog Compounds, Licensed Products and Research Products;

(II) all rights and licenses granted by Takeda hereunder

shall terminate immediately;

(III) if not already completed and provided, Ultragenyx shall complete and provide a report of the Development activities for the Licensed [***] Product in the Takeda Field as set forth in the Initial [***] Development Plan in accordance with Section 4.3(a);

(IV) Ultragenyx, as soon as reasonably practical after the effective date of such termination, shall provide to Takeda, as applicable and to the extent permitted under any applicable Third Party contract, (1) any Information, including copies of all Clinical Trial data and results, and the like developed by or for the benefit of Ultragenyx relating to a Licensed Product or Research Product, and (2) other documents to the extent relating to the Licensed [***] Compounds, Licensed Analog Compounds, [***] Compounds, Candidate Products, Licensed Products or Research Products that are necessary for their Exploitation. Ultragenyx will cooperate with Takeda to provide a transfer of such material Information and documents at Ultragenyx's expense. At Takeda's request, Ultragenyx shall assign to Takeda any and all Patents and agreements to which Ultragenyx, or its Affiliate, and a Third Party are parties, and that govern the Exploitation activities conducted in connection with such Compounds or Products prior to such termination, or, if such assignment is not permitted under the relevant agreement: (i) grant to Takeda other rights to provide to Takeda the benefit of such non- assignable agreement, at Ultragenyx's expense, to the extent permitted under the terms of such non-assignable agreement; or (ii) to the extent not permitted under the terms of such non- assignable agreement, the Parties shall discuss in good faith an alternative solution to enable Takeda to receive, at Ultragenyx's expense, the benefit of the terms of such non-assignable agreement. In addition to the actions contemplated in this Section 15.7(a)(ii)(A)(IV), Ultragenyx shall take such other actions and execute such other instruments, assignments and documents, at Ultragenyx's expense, as may be necessary to effect the transfer of rights to such Compound(s) and Product(s) hereunder to Takeda;

(V) Ultragenyx shall, at its expense, transfer to Takeda any and all Regulatory Documentation related to a Licensed Product or Research Product, including any Product INDs and Product Regulatory Approvals and, upon Takeda's request, shall make available to Takeda any other relevant information reasonably related to such Regulatory Documentation; and

(VI) effective on the date of termination, Ultragenyx, for itself and on behalf of its Affiliates, hereby assigns (and to the extent such assignment can only be made in the future hereby agrees to assign) to Takeda all right, title and interest in and to any Licensed Product Improvements, Licensed Product Improvement Patents, Option Product Improvements, and Option Product Improvement Patents, in each case where Controlled by Ultragenyx or its Affiliates. Ultragenyx will, at its expense, execute and record assignments and other necessary documents consistent with such change in ownership; or

(B) in lieu of actual termination under (A) above, Takeda may elect that all rights and licenses granted to Takeda hereunder shall continue under this Agreement and any milestones or royalty payments that become due to Ultragenyx by Takeda with respect to

any Exercised Product after such termination shall be reduced by fifty percent (50%) and paid to Ultragenyx in accordance with the payment provisions of this Agreement. This Section 15.7(a)(ii)(B) may only be exercised once.

(iii) For clarity, an Exercised Product License Agreement or an Option Product License Agreement shall include termination provisions similar to this Section 15.7(a) and shall otherwise govern the effects of termination of such agreement in its entirety.

(b) **Effects of Termination of a Compound or Product for Safety Reasons.** In the event of a termination of this Agreement with respect to a particular Compound or Product pursuant to Section 15.3 (for the avoidance of doubt, not a Terminated Product) then:

(i) all license rights received by the terminating Party and all obligations of the terminating Party with respect to the terminated Compound or Product shall cease and, with respect to the terminating Party only, this Agreement shall automatically be deemed to be amended to exclude such rights and obligations of the terminating Party with respect to the terminated Compound or Product but shall otherwise survive and continue in effect for the remaining Compounds and Products; and

(ii) the non-terminating Party shall continue to have all rights and obligations under this Agreement with respect to the terminated Compound or Product (including the obligation to make royalty, milestone and other payments to the terminating Party) unless it also elects to terminate the particular Compound or Product pursuant to Section 15.3.

(c) **Effects of Termination with Respect to a Terminated Product.** In the event of termination of this Agreement with respect to a Terminated Product (but not in the case of any termination of this Agreement in its entirety) then:

(i) all rights and licenses granted hereunder by either Party shall automatically be deemed to be amended to exclude the Terminated Product but shall otherwise survive and continue in effect for the remaining Compounds and Products;

(ii) in the case of termination for convenience pursuant to Section 15.4, if an Option Negotiation Period or Takeda Option Negotiation Period is then ongoing, the Term with respect to such Option Product or Exercised Product, as applicable, will automatically extend until the earlier of (A) expiration of such Option Negotiation Period or Takeda Option Negotiation Period, as applicable, or (B) execution of the applicable Option Product License Agreement or Exercised Product License Agreement;

(iii) if the Terminated Product is a Licensed Product, if not already completed and provided, Ultragenyx shall complete and provide a report of the Development activities for the Licensed [***] Product in the Takeda Field as set forth in the Initial [***] Development Plan in accordance with Section 4.3(a);

(iv) Ultragenyx, as soon as reasonably practical after the effective date of such termination, shall provide to Takeda, as applicable and to the extent permitted under any

applicable Third Party contract, (A) any Information, including copies of all Clinical Trial data and results, and the like developed by or for the benefit of Ultragenyx relating to a Terminated Product, and (B) other documents to the extent relating to the Terminated Products that are necessary for their Exploitation. Ultragenyx will cooperate with Takeda to provide a transfer of such material Information and documents. Ultragenyx shall assign to Takeda any and all Patents and agreements to which Ultragenyx, or its Affiliate, and a Third Party are parties, and that govern the Exploitation activities conducted in connection with a Terminated Product prior to such termination, or, if such assignment is not permitted under the relevant agreement: (1) grant to Takeda other rights to provide to Takeda the benefit of such non-assignable agreement to the extent permitted under the terms of such non-assignable agreement; or (2) to the extent not permitted under the terms of such non-assignable agreement, the Parties shall discuss in good faith an alternative solution to enable Takeda to receive the benefit of the terms of such non- assignable agreement. In addition to the actions contemplated in this Section 15.7(c)(iv), Ultragenyx shall take such other actions and execute such other instruments, assignments and documents as may be necessary to effect the transfer of rights to such Terminated Products hereunder to Takeda. Each Party shall bear its own expenses under this Section 15.7(c)(iv);

(v) Ultragenyx shall transfer to Takeda any and all Regulatory Documentation directly and solely related to a Terminated Product, including any Product INDs and Product Regulatory Approvals and, upon Takeda's request, shall make available to Takeda any other relevant information reasonably related to such Regulatory Documentation;

(vi) effective on the date of termination, Ultragenyx, for itself and on behalf of its Affiliates, hereby assigns (and to the extent such assignment can only be made in the future hereby agrees to assign) to Takeda all right, title and interest in and to any Licensed Product Improvements, Licensed Product Improvement Patents, Option Product Improvements, and Option Product Improvement Patents to the extent the foregoing Cover a Terminated Product and are Controlled by Ultragenyx or its Affiliates. Ultragenyx will execute and record assignments and other necessary documents consistent with such change in ownership; and

(vii) Takeda shall have the right to assume all prosecution, maintenance, and enforcement activities with respect to Patents under this Agreement Covering the Terminated Products. Ultragenyx will cooperate with Takeda and provide Takeda with reasonable assistance and cooperation with the prosecution, maintenance, and enforcement activities with respect to such Patents.

(d) **Effect of Termination on Ultragenyx's Put Rights under the Common Stock Purchase Agreement**. Immediately upon (i) written notice of termination of this Agreement in its entirety pursuant to Section 15.2, or 15.6, (ii) written notice of termination of a Licensed Product or Research Product pursuant to Section 15.2, 15.3, 15.4, 15.5, 18.5 or (iii) upon the Ultragenyx [***] License terminating pursuant to Section 4.3(f), Ultragenyx's rights under the Common Stock Purchase Agreement to require the purchase of the Second Tranche Shares and Third Tranche Shares (as such terms are defined in the Common Stock Purchase Agreement) shall be suspended and such rights shall automatically terminate on the effective date of such termination, provided, however, there shall be no suspension or termination of such Ultragenyx

rights under the Common Stock Purchase Agreement to the extent Ultragenyx terminates the Agreement, a Licensed Product or Research Product pursuant to Section 15.2. Where written notice of termination pursuant to Section 15.2 is provided by Takeda, and Ultragenyx cures all material breaches during the Cure Period, the suspension shall be removed on the effective date of such cure.

15.8 **Effect of Expiration**

(a) **Expiration of Collaboration Term.** Upon expiration of the Collaboration Term for a given Research Product:

(i) All rights to such Research Product shall revert to Takeda except for those rights, if any, granted to Ultragenyx under an Option Product License Agreement;

(ii) As soon as reasonably practical after the effective date of expiration of the Collaboration Term for a given Research Product, Ultragenyx shall, except where otherwise provided under an Option Product License Agreement, provide to Takeda, as applicable and to the extent permitted under any applicable Third Party contract (1) any Information, including copies of all Clinical Trial data and results, and the like developed by or for the benefit of Ultragenyx relating to such Research Product and (2) other documents to the extent relating to such Research Product that are necessary for their continued Exploitation. Ultragenyx will cooperate with Takeda to provide a transfer of such material Information and documents. At Takeda's request, Ultragenyx shall assign to Takeda any and all Patents and agreements to which Ultragenyx, or its Affiliate, and a Third Party are parties, and that govern the Exploitation activities conducted in connection with such Research Product prior to such expiration, or if such assignment is not permitted under the relevant agreement: (i) grant to Takeda other rights to provide to Takeda the benefit of such non-assignable agreement to the extent permitted under the terms of such non-assignable agreement; or (ii) to the extent not permitted under the terms of such non-assignable agreement, the Parties shall discuss in good faith an alternative solution to enable Takeda to receive the benefit of the terms of such non-assignable agreement. In addition to the actions contemplated in this Section 15.8(a)(ii), Ultragenyx shall take such other actions and execute such other instruments, assignments and documents as may be necessary to effect the transfer of rights to such Product to Takeda. Each Party shall bear its own expenses under this Section 15.8(a)(ii);

(iii) Ultragenyx shall transfer to Takeda any and all Regulatory Documentation directly and solely related to such Research Product, including any Product INDs and Product Regulatory Approvals and, upon Takeda's request, shall make available to Takeda any other relevant information reasonably related to such Regulatory Documentation; and

(iv) Takeda shall have the right to assume all prosecution, maintenance, and enforcement activities with respect to Patents under this Agreement Covering such Research Product. Ultragenyx will cooperate with Takeda and provide Takeda with reasonable assistance and cooperation with the prosecution, maintenance, and enforcement activities with respect to such Patents.

(b) **Expiration of Licensed Product Royalty Term.** Upon the expiration of the Licensed Product Royalty Term for each Licensed Product in each country in the Territory, Ultragenyx shall have a non-exclusive, fully-paid up and irrevocable license under the Licensed [***] Technology with respect to such Licensed Product in such country in the Ultragenyx Field for Licensed Products.

(c) **Expiration of Exercised Product License Agreement and Option Product License Agreement**. Each Exercised Product License Agreement and Option Product License Agreement shall provide that, upon expiration of the applicable royalty term, Takeda shall have a non-exclusive, fully-paid up and irrevocable license with respect to the Exercised Products and Licensed Option Products, respectively.

15.9 **Remedies.** Notwithstanding anything to the contrary in this Agreement, except as otherwise set forth in this Agreement, termination or expiration of this Agreement shall not relieve the Parties of any liability or obligation which accrued hereunder prior to the effective date of such termination or expiration, nor prejudice either Party's right to obtain performance of any obligation. Each Party shall be free, pursuant to ARTICLE 16, to seek, without restriction as to the number of times it may seek, damages, costs and remedies that may be available to it under Applicable Laws or in equity and shall be entitled to offset the amount of any damages and costs obtained against the other Party in a final determination under Section 16.4, against any amounts otherwise due to such other Party under this Agreement.

15.10 **Survival**. The following provisions shall survive any expiration or termination of this Agreement for the period of time specified therein (or, if no such period is specified, indefinitely): ARTICLE 1 (Definitions); ARTICLE 16 (Dispute Resolution); and ARTICLE 17 (Indemnification); and Sections 4.5 (Records; Disclosure of Data and Results), 6.6(b) (Research Materials Transfer), 11.9, 11.10, 11.11, 11.12, 11.13 (Payment, Taxes, Audit); 12.1 (Ownership of Inventions); 14.1, 14.2, 14.3, 14.4, 14.5, 14.6, 14.7, 14.8 (Confidentiality); 15.7, 15.8, 15.9, 15.10 (Termination); 18.3, 18.7, 18.8, 18.9, 18.10, 18.14, 18.15, 18.16, and 18.17 (Miscellaneous).

ARTICLE 16 – DISPUTE RESOLUTION

16.1 **Exclusive Dispute Resolution Mechanism.** Except for disputes for which a Party has final decision making authority under this Agreement, including Sections 2.1(b)(ii), 2.2(c)(ii) and 12.4, the Parties agree that the procedures set forth in this ARTICLE 16 shall be the exclusive mechanism for resolving any dispute, controversy, or claim between the Parties that may arise from time to time pursuant to this Agreement relating to either Party's rights or obligations hereunder (each, a "Dispute", and collectively, the "Disputes") that is not resolved through good faith negotiation between the Parties.

16.2 **Resolution by Executive Officers.** In the event of any Dispute, the Parties shall first attempt in good faith to resolve such Dispute by negotiation and consultation between themselves. In the event that such Dispute is not resolved on an informal basis within ten (10) Business Days after receipt of writing notice of such Dispute by a Party, either Party may, by written notice to the other Party, refer the Dispute to the Senior Officers of the other Party for

attempted resolution by good faith negotiation within thirty (30) days after such notice is received. Except where exclusive decision-making authority rests with a Party under this Agreement (including Sections 2.1(b)(ii), 2.2(c)(ii) and 12.4), each Party may, in its sole discretion, seek resolution of any and all Disputes that are not resolved under this Section 16.2 using (a) arbitration pursuant Section 16.3 where arbitration pursuant to Section 16.3 is specifically provided for in this Agreement or (b) otherwise, pursuant to Section 16.4.

16.3 **Baseball Arbitration.** Any Dispute for which arbitration pursuant to this Section 16.3 is specifically provided for in this Agreement shall be finally decided by expedited arbitration in accordance with the following abbreviated dispute resolution procedures:

(a) If the Dispute is not resolved within thirty (30) days after referral to the Party's respective Senior Officers pursuant to Section 16.2, either Party may send the other Party a written notice that it wishes to resolve the Dispute by using a neutral Third Party who is an Expert with at least fifteen (15) years of experience in area of the Dispute (the "Neutral Expert"). The date of the other Party's receipt of such written notices shall be the "Notice Date."

(b) Within fifteen (15) Business Days of the Notice Date, each Party shall notify the other Party in writing of its appointed Expert (each, a "Representative Expert"). The Representative Experts for each Party shall jointly appoint the Neutral Expert within fifteen (15) Business Days.

(c) Within ten (10) Business Days after the appointment of the Neutral Expert, each Party shall submit to the other Party and the Neutral Expert a written summary regarding its position with respect to the Dispute. Contemporaneously with the submission of its written summary regarding its position, each Party shall provide the other Party and the Neutral Expert with copies of all documents it relied upon in its written summary; provided that each Party may redact any portion of such documents which are covered by an applicable privilege or do not relate to the subject matter of this Agreement. Within three (3) Business Days of receipt of the other Party's written summary regarding its position, each Party may submit an opposition statement of no more than five (5) pages in length (excluding exhibits and declarations). Neither Party will be allowed to conduct any discovery. Neither Party may have any communications (either written or oral) with the other Party's Representative Experts or the Neutral Expert other than for the sole purpose of engaging the expert panel or as expressly permitted in this Section 16.3; provided, that oral presentations and follow-up written submissions may be made to the Neutral Expert at such Neutral Expert's request. The Neutral Expert may consult in writing with the Representative Experts regarding the submissions made by either Party; provided that both Representative Experts are aware of such consultation and provided an opportunity to respond. Evaluating each Party's written submissions, the Neutral Expert shall, within ten (10) Business Days of receipt of the written opposition statement, select in total, either Takeda's submission or Ultragenyx's submission. Such decision shall be final, binding and not appealable.

(d) The Party whose submission is not selected shall be solely responsible for the expenses and fees of the Neutral Expert and the reasonable costs and fees of the other Party's Representative Expert.

16.4 **Litigation.** Any unresolved Dispute that was subject to Section 16.2, shall be brought exclusively in a court of competent jurisdiction, federal or state, located in New York, New York, and in no other jurisdiction. Each Party hereby consents to personal jurisdiction and venue in, and agrees to service of process issued or authorized by, such court.

16.5 **Preliminary Injunctions.** Notwithstanding anything in this Agreement to the contrary, a Party may seek a temporary restraining order or a preliminary injunction from any court of competent jurisdiction in order to prevent immediate and irreparable injury, loss, or damage on a provisional basis, pending the decision of the arbitrator(s) on the ultimate merits of any Dispute.

16.6 **Patent and Trademark Disputes.** Notwithstanding anything in this Agreement to the contrary, any and all issues regarding the scope, construction, validity, and enforceability of any Patent or trademark relating to a Product that is the subject of this Agreement shall be determined in a court or other tribunal, as the case may be, of competent jurisdiction under the applicable patent or trademark laws of the country in which such Patent or trademark rights were granted or arose.

16.7 **Confidentiality.** Any and all activities conducted under ARTICLE 16, including any and all proceedings and decisions under Section 16.4, shall be deemed Confidential Information of each of the Parties, and shall be subject to ARTICLE 14.

16.8 **WAIVER OF RIGHT TO JURY TRIAL**. In connection with the Parties' rights under Section 16.4, EACH PARTY, TO THE EXTENT PERMITTED BY APPLICABLE LAWS, KNOWINGLY, VOLUNTARILY, AND INTENTIONALLY WAIVES ITS RIGHT TO A TRIAL BY JURY IN ANY ACTION OR OTHER LEGAL PROCEEDING ARISING OUT OF OR RELATING TO THIS AGREEMENT AND THE TRANSACTIONS IT CONTEMPLATES. THIS WAIVER APPLIES TO ANY ACTION OR LEGAL PROCEEDING, WHETHER SOUNDING IN CONTRACT, TORT, OR OTHERWISE.

ARTICLE 17 – INDEMNIFICATION

17.1 **Indemnification by Ultragenyx.** Ultragenyx hereby agrees to defend, indemnify and hold harmless Takeda and its Affiliates, and each of their respective directors, officers, employees, agents and representatives (each, a "Takeda Indemnitee") from and against any and all claims, suits, actions, demands, liabilities, expenses and/or loss, including reasonable legal expense and attorneys' fees (collectively, the "Losses"), to which any Takeda Indemnitee may become subject as a result of any claim, demand, action or other proceeding by any Third Party (each, a "Claim") to the extent such Losses arise directly or indirectly out of: (i) the practice by Ultragenyx or its Affiliate of any license granted to it under ARTICLE 3; (ii) the Exploitation of a Compound or a Product by Ultragenyx, its Affiliates or its sublicensees on or after the Effective Date, including, for the avoidance of doubt, any Product Liabilities arising from the use of a Product in the Licensed Field in the Territory on or after the Effective Date and any Losses that may arise due to Ultragenyx, its Affiliates or its sublicensees continuing to Exploit a Compound or Product in its territory or field that is the subject matter of a termination by Takeda pursuant to Section 15.3; (iii) the Exploitation of any Ultragenyx Pipeline Product by Ultragenyx, its Affiliates or its licensees before the Effective Date, including, for the avoidance

of doubt, any Product Liabilities arising from the use of a Ultragenyx Pipeline Product; (iv) the breach by Ultragenyx of any warranty, representation, covenant or agreement made by Ultragenyx in this Agreement; (v) the negligence, gross negligence or willful misconduct (including to the extent such negligence, gross negligence or willful misconduct gives rise to Product Liabilities under any legal theory) of Ultragenyx, its Affiliate or its sublicensee, or any officer, director, employee, agent or representative thereof; except, with respect to each of subsections (i) through (v) above, to the extent such Losses arise directly or indirectly from the negligence, gross negligence or willful misconduct of any Takeda Indemnitee or the breach by Takeda of any warranty, representation, covenant or agreement made by Takeda in this Agreement. Notwithstanding the foregoing, following the execution of an Exercised Product License Agreement or Option Product License Agreement, the terms of such license agreement shall govern the indemnification terms with respect to such Product(s) that are the subject of such license agreement.

17.2 **Indemnification by Takeda.** Takeda hereby agrees to defend, indemnify and hold harmless Ultragenyx and its Affiliates and each of their respective directors, officers, employees, agents and representatives (each, an "Ultragenyx Indemnitee") from and against any and all Losses to which any Ultragenyx Indemnitee may become subject as a result of any Claim to the extent such Losses arise directly or indirectly out of: (i) the practice by Takeda or its Affiliate of any license granted to it under ARTICLE 3; (ii) the Exploitation of a Product by Takeda, its Affiliates or its sublicensees on or after the Effective Date, including, for the avoidance of doubt, any Product Liabilities arising from the use on or after the Effective Date of a Licensed [***] Product in the Takeda Field in the Territory and any Losses that may arise due to Takeda, its Affiliates or its sublicensees continuing to Exploit a Compound or Product in its territory or field that is the subject matter of a termination by Ultragenyx pursuant to Section 15.3; (iii) the Exploitation of any Licensed [***] Product, [***] Product or Candidate Product by Takeda, its Affiliates or its licensees before the Effective Date, including, for the avoidance of doubt, any Product Liabilities arising from the use of a Licensed [***] Product, [***] Product or Candidate Product by Takeda, its Affiliates or its licensees before the Effective Date, (iv) the breach by Takeda of any warranty, representation, covenant or agreement made by Takeda in this Agreement; (iv) the negligence, gross negligence or willful misconduct (including to the extent such negligence, gross negligence or willful misconduct gives rise to product liability Claims under any legal theory) of Takeda or its Affiliate or its licensee (other than Ultragenyx or its Affiliate or sublicensee), or any officer, director, employee, agent or representative thereof; except, with respect to each of subsections (i) through (iv) above, to the extent such Losses arise directly or indirectly from the negligence, gross negligence or willful misconduct of any Ultragenyx Indemnitee or the breach by Ultragenyx of any warranty, representation, covenant or agreement made by Ultragenyx in this Agreement. Notwithstanding the foregoing, following the execution of an Exercised Product License Agreement or Option Product License Agreement, the terms of such license agreement shall govern the indemnification terms with respect to such Product(s) that are the subject of such license agreement.

17.3 **Indemnification Procedures**.

(a) **Notice.** Promptly after a Takeda Indemnitee or an Ultragenyx Indemnitee (each, an "Indemnitee") receives notice of a pending or threatened Claim, such Indemnitee shall give written notice of the Claim to the Party from whom the Indemnitee is entitled to receive indemnification pursuant to Sections 17.1 or 17.2, as applicable (the "Indemnifying Party"). However, an Indemnitee's delay in providing or failure to provide such notice will not relieve the Indemnifying Party of its indemnification obligations, except to the extent it can demonstrate prejudice due to the delay or lack of notice.

(b) **Defense.** Upon receipt of notice under Section 17.3(a) from the Indemnitee, the Indemnifying Party will have the duty to either compromise or defend, at its own expense and by counsel (reasonably satisfactory to Indemnitee), such Claim. The Indemnifying Party will promptly (and in any event not more than twenty (20) days after receipt of the Indemnitee's original notice) notify the Indemnitee in writing that it acknowledges its obligation to indemnify the Indemnitee with respect to the Claim pursuant to this ARTICLE 17 and of its intention either to compromise or defend such Claim. Once the Indemnifying Party gives such notice to the Indemnitee, the Indemnifying Party is not liable to the Indemnitee for the fees of other counsel or any other expenses subsequently incurred by the Indemnitee in connection with such defense, other than the Indemnitee's reasonable costs of investigation and cooperation. However, the Indemnitee will have the right to employ separate counsel and to control the defense of a Claim at its own expense.

(c) **Cooperation.** The Indemnitee will cooperate fully with the Indemnifying Party and its legal representatives in the investigation and defense of any Claim. The Indemnifying Party will keep the Indemnitee informed on a reasonable and timely basis as to the status of such Claim (to the extent the Indemnitee is not participating in the defense of such Claim) and conduct the defense of such Claim in a prudent manner.

(d) **Settlement.** If an Indemnifying Party assumes the defense of a Claim, no compromise or settlement of such Claim may be effected by the Indemnifying Party without the Indemnitee's written consent (which consent will not be unreasonably withheld, conditioned or delayed), unless: (i) there is no finding or admission of any violation of law or any violation of the rights of any person and no effect on any other claims that may be made against the Indemnitee; (ii) the sole relief provided is monetary damages that are paid in full by the Indemnifying Party; and (iii) the Indemnitee's rights under this Agreement are not adversely affected. If the Indemnifying Party fails to assume defense of a Claim within a reasonable time, the Indemnitee may settle such Claim on such terms as it deems appropriate with the consent of the Indemnifying Party (which consent shall not be unreasonably withheld, conditioned or delayed), and the Indemnifying Party will be obligated to indemnify the Indemnitee for such settlement as provided in this ARTICLE 17.

17.4 **Insurance.** Each Party shall, at its own expense, procure and maintain during the Term and for a period of five (5) years thereafter, insurance policy/policies, including product liability insurance, adequate to cover its obligations hereunder and which are consistent with normal business practices of prudent companies similarly situated. Such insurance shall not be construed to create a limit of a Party's liability with respect to its indemnification obligations

under this ARTICLE 17. Each Party shall provide the other Party with written evidence of such insurance or self-insurance upon request. Each Party shall provide the other Party with prompt written notice of cancellation, non-renewal or material change in such insurance or self- insurance that could materially adversely affect the rights of such other Party hereunder, and shall provide such notice within thirty (30) days after any such cancellation, non-renewal or material change.

17.5 **Limitation of Liability.** EXCEPT FOR A PARTY'S OBLIGATIONS SET FORTH IN THIS ARTICLE 17, AND ANY BREACH OF ARTICLE 14 (CONFIDENTIALITY)**,** IN NO EVENT WILL EITHER PARTY BE LIABLE TO THE OTHER PARTY (OR THE OTHER PARTY'S AFFILIATES OR SUBLICENSEES) IN CONNECTION WITH THIS AGREEMENT FOR LOST REVENUE, LOST PROFITS, LOST SAVINGS, LOSS OF USE, DAMAGE TO GOODWILL, OR ANY CONSEQUENTIAL, INCIDENTAL, SPECIAL, EXEMPLARY, PUNITIVE OR INDIRECT DAMAGES UNDER ANY THEORY, INCLUDING CONTRACT, NEGLIGENCE, OR STRICT LIABILITY, EVEN IF THAT PARTY HAS BEEN PLACED ON NOTICE OF THE POSSIBILITY OF SUCH DAMAGES.

ARTICLE 18 – MISCELLANEOUS

18.1 HSR Act.

(a) Each of Ultragenyx and Takeda shall, within ten (10) Business Days after Execution Date, file with the United States Federal Trade Commission and the Antitrust Division of the United States Department of Justice, any HSR Filing required of it under the HSR Act with respect to the subject matter of this Agreement, which forms shall specifically request early termination of the initial HSR Act waiting period. The Parties will cooperate with one another to the extent necessary in the preparation of any such HSR Filing. The Parties hereto commit to instruct their respective counsel to cooperate with each other and use good faith, diligent efforts to facilitate and expedite the identification and resolution of any such issues and, consequently, the expiration of the applicable HSR Act waiting period, such good faith diligent efforts to include counsel's undertaking: (i) to keep each other appropriately informed of communications received from and submitted to personnel of the reviewing antitrust authority; and (ii) to confer with each other regarding appropriate contacts with and response to personnel of the United States Federal Trade Commission and the Antitrust Division of the United States Department of Justice. Each Party will be responsible for its own costs and expenses and Ultragenyx will be responsible for all filing fees associated with any HSR Filing. In respect of any HSR Filing, each of Ultragenyx and Takeda will use its good faith, diligent efforts to eliminate any concern on the part of any court or governmental authority regarding the legality of the proposed transaction, including cooperating in good faith with any government investigation and the prompt production of documents, information, and witnesses requested in the course of such of any such investigation, including those contained in a Request for Additional Information and Documentary Materials (as that term is defined in the HSR Act), and to cause the Effective Date of this Agreement to occur as soon as practical, as provided in Section 18.1(b). Nothing in this Section shall require either Party to consent to the divestiture or other disposition of any of its or its Affiliates' assets or to consent to any other structural or conduct remedy, and each Party and

its Affiliates shall have no obligation to contest, administratively or in court, any ruling, order or other action of the United States Federal Trade Commission and the Antitrust Division of the United States Department of Justice or any Third Party respecting the transactions contemplated by this Agreement.

(b) Except for the specific provisions expressly identified in Section 18.1(c), this Agreement shall not be effective until the (i) the HSR Conditions are met and (ii) the earlier of (A) the date on which the Tax Conditions are met, or (B) July 18, 2016, at which time this Agreement shall be effective automatically in its entirety (such date the "**Effective Date**").

(c) Notwithstanding Section 18.1(b) and anything in this Agreement to the contrary, the following provisions of this Agreement shall be in full force and effect as of the Execution Date: Sections 14.5 (Publicity) and 14.6 (Securities Filings), ARTICLE 1 (Definitions) and ARTICLE 18 (other than Sections 18.2, 18.5 and 18.6) (Miscellaneous).

(d) If the Effective Date has not occurred within one hundred eighty (180) days following the Execution Date, or such date as the Parties may mutually agree, this Agreement may be terminated by either Party on written notice to the other.

18.2 **Exports and Restrictions on Competition**.

(a) **Exports**. Except as provided in this Agreement, each Party shall not, and shall cause its Affiliates and sublicensees not to, whether directly or indirectly through a Third Party, export, distribute or sell:

(i) in the case of Ultragenyx, (A) Licensed [***] Products outside the Ultragenyx Field or outside the Territory, (B) Licensed Analog Products outside the Licensed Field or outside the Territory, (C) Research Products unless and until an Option Product License Agreement is executed for such Products and then only in accordance with such Option Product License Agreement; provided further that, if the Takeda Option has been exercised for a given Product Ultragenyx may not export, distribute or sell such Product in the Takeda Territory.

(ii) In the case of Takeda, Ultragenyx Pipeline Products outside of the Takeda Territory.

(b) [***] **Obligations**. Ultragenyx shall not, and shall cause its Affiliates not to, whether directly or indirectly through a Third Party (including any sublicensee), (i) [***] or (ii) [***]. Ultragenyx shall not be in breach of this Section 18.2(b) by acquiring, merging or consolidating with a Third Party which develops or commercializes [***]; provided, however, that in the event Ultragenyx acquires such [***], it must, unless Takeda agrees to the contrary, within [***] of such acquisition, either divest such [***] to a Third Party, [***], or, if applicable, terminate

this Agreement [***] in accordance with Section 15.4.

18.3 **Notice.** Any notice, request, or other communication permitted or required under this Agreement shall be in writing, shall refer specifically to this Agreement and shall be hand delivered or sent by a recognized overnight delivery service, costs prepaid, or by facsimile (with transmission confirmed), to the following addresses or to such other addresses as a Party may designate by written notice in accordance with this Section 18.3:

If to Takeda:

Takeda Pharmaceutical Company Limited 1-1, Doshomachi 4-
chome,
Chuo-ku, Osaka 540-8645
Attention: Head of Global Business Development Facsimile: (+81) 3-3278-2323

Copy to:

Takeda Pharmaceuticals U.S.A., Inc. One Takeda Parkway
Deerfield, IL 60015
Attention: General Counsel, Legal Department Facsimile: 224-554-7831

If to Ultragenyx:

Ultragenyx Pharmaceutical Inc. 60 Leveroni Court
Novato, CA 94949
Attention: Chief Business Officer

Copy to:

Cooley LLP
3175 Hanover Street Palo Alto,
CA 94304 Attention: Glen Sato
Fax: 650-849-7400

18.4 **Designation of Affiliates**. Each Party may discharge any obligations and exercise any rights hereunder through delegation of its obligations or rights to any of its Affiliates. Each Party hereby guarantees the performance by its Affiliates of such Party's obligations under this Agreement, and shall cause its Affiliates to comply with the provisions of this Agreement in connection with such performance. Any breach by a Party's Affiliate of any of such Party's obligations under this Agreement shall be deemed a breach by such Party, and the other Party

may proceed directly against such Party without any obligation to first proceed against such Party's Affiliate.

18.5 **Change of Control of Ultragenyx**.

(a) **Notice**. Ultragenyx (or its successor) shall provide notice to Takeda of any Change of Control of Ultragenyx within [***] Business Days after the date upon which the Ultragenyx Change of Control closes or otherwise becomes effective.

(b) **Effects of Change of Control of Ultragenyx**. In the event of a Change of Control of Ultragenyx, the following shall apply:

(i) The [***] applicable in the event of a Change of Control of Ultragenyx shall apply.

(ii) On or before the date that is [***] days after the date upon which a Change of Control of Ultragenyx closes or otherwise becomes effective, Takeda may take or require that Ultragenyx, or its successor, take or perform, as applicable, any one or more of the following actions: (A) Ultragenyx and its successor shall adopt [***], approved by [***], to prevent [***], (B) the [***] shall be [***] to be limited to those [***] as of the effective date of the Ultragenyx Change of Control, provided that if [***] has [***] shall be [***], (C) [***] shall be amended to require [***] written consent in order for [***] thereunder to the extent [***], and (D) [***] may [***], one or more of [***], in which case any [***] under [***] shall [***] and any [***] designated by [***] shall be deemed [***]; provided that to the extent that [***] in connection with the [***] on or before such date, such [***], as applicable, and associated [***] and such [***] shall not be deemed [***] under this Section 18.5(b)(ii). For clarity, [***] pursuant to this Section 18.5(b)(ii) shall not [***].

18.6 **Force Majeure.** Both Parties shall be excused from the performance of their obligations under this Agreement to the extent that such performance is prevented by Force Majeure and the nonperforming Party promptly provides notice of the prevention to the other Party. Such excuse shall be continued so long as the condition constituting Force Majeure continues and the nonperforming Party takes reasonable efforts to remove the condition. Notwithstanding the foregoing, a Party shall not be excused from making payments owed hereunder because of a Force Majeure affecting such Party. If a Force Majeure persists for more than ninety (90) days,

then the Parties will discuss in good faith the modification of the Parties' obligations under this Agreement in order to mitigate the delays caused by such Force Majeure.

18.7 **Assignment.** Prior to the Effective Date, neither Party may assign or transfer this Agreement or any rights or obligations hereunder without the prior written consent of the other. On or after the Effective Date, neither Party may assign or transfer this Agreement or any rights or obligations hereunder without the prior written consent of the other; provided that no such consent is required for (a) assignment to Affiliates or (b) in connection with the sale of all or substantially all of the assets to which this Agreement relates, whether in a merger, sale of stock, sale of assets or any other transaction (subject, in the case of Ultragenyx, to Section 18.5). Any successor or assignee of rights and/or obligations permitted hereunder shall, in writing to the other Party, expressly assume performance of such rights and/or obligations. Any permitted assignment shall be binding on the successors of the assigning Party. Any assignment or attempted assignment by either Party in violation of the terms of this Section shall be null, void and of no legal effect.

18.8 **Severability.** If any one or more of the provisions of this Agreement is held to be invalid or unenforceable by any court of competent jurisdiction from which no appeal can be or is taken, the provision shall be considered severed from this Agreement and shall not serve to invalidate any remaining provisions hereof. The Parties shall make a good faith effort to replace any invalid or unenforceable provision with a valid and enforceable one such that the objectives contemplated by the Parties when entering this Agreement may be realized.

18.9 **English Language.** This Agreement shall be written and executed in, and all other communications under or in connection with this Agreement, shall be in the English language. Any translation into any other language shall not be an official version thereof, and in the event of any conflict in interpretation between the English version and such translation, the English version shall control.

18.10 **Waiver and Non-Exclusion of Remedies.** Any term or condition of this Agreement may be waived at any time by the Party that is entitled to the benefit thereof, but no such waiver shall be effective unless set forth in a written instrument duly executed by or on behalf of the Party waiving such term or condition. The waiver by either Party hereto of any right hereunder or of the failure to perform or of a breach by the other Party shall not be deemed a waiver of any other right hereunder or of any other breach or failure by such other Party whether of a similar nature or otherwise. The rights and remedies provided herein are cumulative and do not exclude any other right or remedy provided by Applicable Laws or otherwise available except as expressly set forth herein.

18.11 **Further Assurance.** Each Party shall duly execute and deliver, or cause to be duly executed and delivered, such further instruments and do and cause to be done such further acts and things, including the filing of such assignments, agreements, documents, and instruments, as may be necessary or as the other Party may reasonably request in connection with this Agreement or to carry out more effectively the provisions and purposes hereof.

18.12 **Relationship of the Parties.** It is expressly agreed that Takeda, on the one hand, and Ultragenyx, on the other hand, shall be independent contractors and that the relationship between the two Parties shall not constitute a partnership, joint venture or agency. Neither Takeda nor Ultragenyx shall have the authority to make any statements, representations or commitments of any kind, or to take any action which shall be binding on the other, without the prior written consent of the other Party to do so. All persons employed by a Party shall be employees of that Party and not of the other Party and all costs and obligations incurred by reason of such employment shall be for the account and expense of such Party. For clarity, (a) if Takeda provides Research Support for an Ultragenyx Pipeline Product (other than Exercised Products) or Licensed Option Product (in connection with an Option Product License Agreement), Takeda shall be deemed an independent contractor in the performance of such Research Support and (b) in no case shall Takeda provide Research Support with respect to a Licensed Product.

18.13 **Counterparts.** This Agreement may be executed in two (2) or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. This Agreement may be executed by facsimile, .pdf or other electronically transmitted signatures and such signatures shall be deemed to bind each Party hereto as if they were the original signatures.

18.14 **Construction.** Except where the context otherwise requires, wherever used, the singular shall include the plural, the plural the singular, and the use of any gender shall be applicable to all genders. Whenever this Agreement refers to a number of days, such number refers to calendar days. The terms “including,” “include,” or “includes” as used herein shall mean “including, but not limited to,” and shall not limit the generality of any description preceding such term. The language of this Agreement shall be deemed to be the language mutually chosen by the Parties and no rule of strict construction shall be applied against either Party hereto. Each Party represents that it has been represented by legal counsel in connection with this Agreement and acknowledges that it has participated in the drafting hereof. In interpreting and applying the terms and provisions of this Agreement, the Parties agree that no presumption will apply against the Party which drafted such terms and provision.

18.15 **Governing Laws.** This Agreement was prepared in the English language, which language shall govern the interpretation of, and any dispute regarding, the terms of this Agreement. This Agreement and all disputes arising out of or related to this Agreement or any breach hereof shall be governed by and construed under the laws of the State of New York, without giving effect to any choice of law principles that would require the application of the laws of a different state.

18.16 **Entire Agreement.** This Agreement, including the Exhibits hereto, and the Common Stock Purchase Agreement set forth the complete, final and exclusive agreement and all the covenants, promises, agreements, warranties, representations, conditions and understandings between the Parties hereto with respect to the subject matter hereof and supersedes, as of the Execution Date, all prior and contemporaneous agreements and understandings between the Parties with respect to the subject matter hereof; provided, that, until the Effective Date, the Confidentiality Agreement shall continue in full force and effect in accordance with its terms.

Except as provided in the Common Stock Purchase Agreement, there are no covenants, promises, agreements, warranties, representations, conditions or understandings, either oral or written, between the Parties other than as are set forth herein and therein. No subsequent alteration, amendment, change or addition to this Agreement shall be binding upon the Parties unless reduced to writing and signed by an authorized officer of each Party. In the event of any inconsistency between the body of this Agreement and the Exhibits to this Agreement, the Common Stock Purchase Agreement, or any subsequent agreements ancillary to this Agreement, unless otherwise expressly stated to the contrary in such Exhibit, Common Stock Purchase Agreement or subsequent ancillary agreement, the terms contained in this Agreement shall control.

18.17 **Headings.** The headings of each Article and Section in this Agreement have been inserted for convenience of reference only and are not intended to limit or expand on the meaning of the language contained in the particular Article or Section.

SIGNATURE PAGE FOLLOWS

THIS AGREEMENT is executed by the authorized representatives of the Parties as of the Execution Date.

ULTRAGENYX PHARMACEUTICAL INC.	**TAKEDA PHARMACEUTICALCOMPANY LIMITED**
By /s/ Emil Kakkis	By /s/ Misako Hamamura
Name: Emil Kakkis	Name: Misako Hamamura
Title: CEO	Title: Head of JP Strategy & BD

Exhibit 1.6(i)

[***]

Chemical Name: [***]

Molecular Formula: [***]
Molecular Weight: [***]

Exhibit 1.6(iii)

[***]

CONFIDENTIAL TREATMENT REQUESTED
Certain information in this document has been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment has been requested with respect to omitted portions marked "***".

Exhibit 1.82

Initial [***] **Development Plan**

Initial Development Plan Framework

[***]

Estimated Timeline

[***]

Development Activities and Budget

[***]

Exhibit 1.91 Knowledge Group

Ultragenyx Position Titles

Tom Kassberg, SVP and Chief Business Officer Shalini Sharp, SVP and Chief Financial Officer Sunil Agarwal, SVP and Chief Medical Officer Cori Leonard, VP, Regulatory
Yael Weiss, Executive Director, Search and Evaluation, Business Development Rob Anstey, Senior Director, Business Development

Takeda Position Titles

[***]

Exhibit 1.94

[***]

- Chemical Name: [***]
- Molecular Formula: [***]
- Molecular Weight: [***]

Exhibit 1.99

Licensed Analog Compounds

[***]

Exhibit 1.137

Preexisting Third Party IP

[***]

CONFIDENTIAL TREATMENT REQUESTED

Certain information in this document has been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment has been requested with respect to omitted portions marked "***".

Exhibit 1.141

Product INDs

[***]

CONFIDENTIAL TREATMENT REQUESTED

Certain information in this document has been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment has been requested with respect to omitted portions marked "***".

Exhibit 1.168
Takeda Patents

Licensed [***] **Patent**

Patent / Publication	**Priority / *Application***	**Inventor(s) / Assignee(s)**	**Title / Claims**	**Status**
[***]	[***]	[***]	[***]	[***]

Exhibit 1.188
Ultragenyx Patents

Ultragenyx [***] **Patents**

[***]

Ultragenyx [***] Patents

[***]

Exhibit 1.195
[***]

CONFIDENTIAL TREATMENT REQUESTED
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Exhibit 6.1
Listed Compounds
[***]

Exhibit 6.3(a)
[***] Research Plan
[***]

CONFIDENTIAL TREATMENT REQUESTED
Certain information in this document has been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment has been requested with respect to omitted portions marked "***".

Exhibit 6.10(b)

[***]

CONFIDENTIAL TREATMENT REQUESTED

Certain information in this document has been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment has been requested with respect to omitted portions marked "***".

Exhibit 13.2(b)

[***]

CONFIDENTIAL TREATMENT REQUESTED

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Exhibit 14.5
Form of Press Release

Contact Ultragenyx Pharmaceutical Inc. Investors & Media
Ryan Martins 844-758-7273

For Takeda Pharmaceutical Company Limited: Tsuyoshi Tada – Japan
tsuyoshi.tada@takeda.com
+81332782417

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+1-224-554-7681

Ultragenyx and Takeda enter into a Collaboration to Develop and Commercialize Therapies for Rare Genetic Diseases

Ultragenyx to license and develop one or more product candidates from Takeda Takeda to make equity investment in Ultragenyx to fund development

NOVATO, CA, June 7, 2016 and OSAKA, JAPAN, June 8, 2016 – Ultragenyx Pharmaceutical Inc. (NASDAQ: RARE), a biopharmaceutical company focused on the development of novel products for rare and ultra- rare genetic diseases, and Takeda Pharmaceutical Company Limited (TSE: 4502), today announced a strategic partnership to develop and commercialize therapies to treat rare genetic diseases.

Ultragenyx will initially receive an exclusive license to one preclinical Takeda product candidate in a pre- determined field of use, and will have an exclusive option to co-develop and co-commercialize the product candidate in additional therapeutic areas. The companies have also established a five-year research collaboration in which Ultragenyx will have the option to license up to five additional Takeda

product candidates for rare diseases after the parties agree on and conduct initial validation activities under the purview of a Joint Research Committee.

“This broad collaboration provides Ultragenyx with a product opportunity that is approaching clinical- stage development as well as a potential continued source of new product candidates that will help us achieve our goal of bringing a new therapy into the clinic every one to two years,” said Emil D. Kakkis, MD, PhD, Chief Executive Officer of Ultragenyx. “Takeda has an impressive early pipeline of therapies with potential across a number of rare genetic diseases, and we are pleased that Takeda has chosen to partner with us to bring these therapies to patients with rare diseases that have few or no treatment options.”

"Ultragenyx is a rapidly emerging rare disease company, led by a highly experienced and successful management team," said Andrew Plump, M.D., Ph.D., Chief Medical and Scientific Officer of Takeda. “This partnership provides Takeda access to Ultragenyx’s strong patient-centric development and regulatory capabilities in the rare disease space, and could create significant value for both companies by delivering important new therapies to patients.”

Takeda will receive an exclusive option to commercialize any licensed products resulting from the collaboration in Asia, including Japan. In addition, Takeda receives an option to exclusively license one Ultragenyx pipeline product in Japan. Each company will receive potential development and sales milestone payments and royalties on net sales of licensed products by the other party.

Takeda will invest up to $65 million in Ultragenyx in two tranches, the first of which will comprise a $25million stock purchase along with a $15 million cash premium at closing. This will be followed at Ultragenyx’s option, within 12 months, by a second equity purchase of $25million with no additional premium. A potential third equity investment by Takeda is contingent upon Ultragenyx achieving a specific development milestone on a second asset. No additional financial details were disclosed.

The completion of the transactions are subject to Hart-Scott-Rodino Antitrust Improvements Act of 1976 (HSR) review and the satisfaction of other customary closing conditions.

About Ultragenyx

Ultragenyx is a clinical-stage biopharmaceutical company committed to bringing to market novel products for the treatment of rare and ultra-rare diseases, with a focus on serious, debilitating genetic diseases. Founded in 2010, the company has rapidly built a diverse portfolio of product candidates with the potential to address diseases for which the unmet medical need is high, the biology for treatment is clear, and for which there are no approved therapies.

The company is led by a management team experienced in the development and commercialization of rare disease therapeutics. Ultragenyx’s strategy is predicated upon time and cost-efficient drug development, with the goal of delivering safe and effective therapies to patients with the utmost urgency.

For more information on Ultragenyx, please visit the company's website at www.ultragenyx.com.

About Takeda

Takeda Pharmaceutical Company Limited (TSE: 4502) is a global, R&D-driven pharmaceutical company committed to bringing better health and a brighter future to patients by translating science into life- changing medicines. Takeda focuses its research efforts on oncology, gastroenterology and central nervous system therapeutic areas. It also has specific development programs in specialty cardiovascular diseases as well as late-stage candidates for vaccines. Takeda conducts R&D both internally and with partners to stay at the leading edge of innovation. New innovative products, especially in oncology, central nervous system and gastroenterology, as well as its presence in emerging markets, fuel the growth of Takeda. More than 30,000 Takeda employees are committed to improving quality of life for patients, working with our partners in health care in more than 70 countries. For more information, visit http://www.takeda.com/news.

Ultragenyx Forward-Looking Statements

Except for the historical information contained herein, the matters set forth in this press release, including statements regarding the potential to develop the licensed product candidate in additional therapeutic areas, as well as the potential to develop additional rare disease targets pursuant to the collaboration and the ability to bring new therapies to clinic, are forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. Such forward-looking statements involve substantial risks and uncertainties that could cause our development programs, future results, performance or achievements to differ significantly from those expressed or implied by the forward-looking statements. Such risks and uncertainties include, among others, the satisfaction of the HSR requirements and the impact on the timing of the closing, whether any products will be successfully developed and commercialized from the collaboration, uncertainties inherent in the drug development process and other matters that could affect the potential for success of the collaboration, including the sufficiency of existing cash, cash equivalents and short-term investments to fund operations. Ultragenyx undertakes no obligation to update or revise any forward-looking statements. For a further description of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to the business of the company in general, see Ultragenyx's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on March 10 2016, and its subsequent periodic reports filed with the Securities and Exchange Commission.

Takeda Forward-Looking Statements

This press release contains "forward-looking statements." Forward-looking statements include all statements other than statements of historical fact, including plans, strategies and expectations for the future, statements regarding the expected timing of filings and approvals relating to the transaction, the expected timing of the completion of the transaction, the ability to complete the transaction or to satisfy the various closing conditions, future revenues and profitability from or

growth or any assumptions underlying any of the foregoing. Statements made in the future tense, and words such as "anticipate," "expect," "project," "continue," "believe," "plan," "estimate," "pro forma," "intend," "potential," "target," "forecast," "guidance," "outlook," "seek," "assume," "will," "may," "should," and similar expressions are intended to qualify as forward-looking statements. Forward-looking statements are based on estimates and assumptions made by management that are believed to be reasonable, though they are inherently uncertain and difficult to predict. Investors and security holders are cautioned not to place undue reliance on these forward-looking statements.

Forward-looking statements involve risks and uncertainties that could cause actual results or experience to differ materially from that expressed or implied by the forward-looking statements. Some of these risks and uncertainties include, but are not limited to: required regulatory approvals for the transaction may not be obtained in a timely manner, if at all; the conditions to closing of the transaction may not be satisfied; competitive pressures and developments; applicable laws and regulations; the success or failure of product development programs; actions of regulatory authorities and the timing thereof; changes in exchange rates; and claims or concerns regarding the safety or efficacy of marketed products or product candidates in development.

The forward-looking statements contained in this press release speak only as of the date of this press release, and neither Ultragenyx nor Takeda undertakes any obligation to revise or update any forward-looking statements to reflect new information, future events or circumstances after the date of the forward-looking statement. If one or more of these statements is updated or corrected, investors and others should not conclude that additional updates or corrections will be made.

COMMON STOCK PURCHASE AGREEMENT

THIS COMMON STOCK PURCHASE AGREEMENT (this "**Agreement**") is entered into as of June 6, 2016, by and among Ultragenyx Pharmaceutical Inc., a Delaware corporation (the "**Company**"), and Takeda Pharmaceutical Company Limited, a Japanese corporation ("**Purchaser**").

WHEREAS, the Company desires to issue and sell to Purchaser up to Seventy Five Million Dollars ($75,000,000) worth of shares (the "**Shares**") of common stock, par value $0.001 per share, of the Company (the "**Common Stock**"), which Shares shall be authorized and issued in accordance with the terms of this Agreement (the "**Common Stock Financing**");

WHEREAS, prior to or concurrently with the consummation of the transactions contemplated hereby, and as a condition to the willingness of, and material inducement to, Purchaser to enter into this Agreement, the Company and Purchaser shall enter into a Collaboration and License Agreement of even date herewith (the "**Collaboration Agreement**"); and

WHEREAS, subject to the terms and conditions set forth in this Agreement, Purchaser desires to purchase from the Company the Shares.

NOW, THEREFORE, in consideration of the mutual promises, representations, warranties, covenants and conditions set forth in this Agreement, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the parties hereto hereby agree as follows:

1. PURCHASE AND SALE

1.1 **Sale and Issuance of Shares.** In consideration of the Collaboration Agreement and in express reliance upon the representations, warranties and covenants set forth herein, and subject to the terms and conditions set forth in this Agreement, the Company shall issue and sell to Purchaser, and Purchaser shall purchase from the Company, the Shares; *provided* that in no event shall the aggregate number of Shares subject to issuance pursuant to this Section 1 exceed twenty percent (20%) of the total outstanding shares of the Company's Common Stock calculated as of the Initial Closing (as defined below).

1.2 **Initial Closing.** The initial purchase and sale of the Shares shall take place remotely via the exchange of documents and signatures at 10:00 a.m. on the Effective Date, as defined in the Collaboration Agreement (the "**Effective Date**"), or at such other time as the Company and Purchaser shall mutually agree (which time, date and place are referred to in this Agreement as the "**Initial Closing**"). At the Initial Closing, the Company shall instruct American Stock Transfer & Trust Company, LLC (the "**Transfer Agent**") to register the issuance of the Initial Closing Shares (as defined below) via book entry, against delivery to the Company by Purchaser at the Initial Closing of Forty Million Dollars ($40,000,000) (the "**Initial Closing Consideration**"), payable in immediately available funds by wire transfer to an account or accounts designated by the Company. The "**Initial Closing Shares**" shall mean that number of shares of Common Stock equal to Twenty Five Million ($25,000,000) divided by the Bloomberg volume-weighted average price for a share of Common Stock on the NASDAQ Global Select Market for the 30 trading day period ending on the last day on which the NASDAQ Global Select Market is open (a "**Trading Day**") prior to the Execution Date, as defined in the Collaboration Agreement, rounded to the nearest whole share. For the avoidance of doubt, the Initial Closing Consideration represents Twenty Five Million Dollars ($25,000,000) worth of Common Stock plus a Fifteen Million Dollar ($15,000,000) premium, which premium represents the consideration paid in return for certain rights under the Collaboration Agreement, including rights under Sections 8.1 and 8.3 of the Collaboration Agreement.

1.3 **Second Tranche Closing.** During the period beginning on the three-month anniversary of the Effective Date and ending on the one-year anniversary thereof, the Company shall have the right, but not the obligation, to direct Purchaser, by its delivery to Purchaser of a Second Tranche Notice (as defined below), to purchase the Second Tranche Shares (as defined below) pursuant to this Section 1.3, and Purchaser thereupon shall have the obligation to purchase the Second Tranche Shares, subject to the conditions set forth in this Agreement, provided that the Collaboration Agreement has not been suspended or terminated in accordance with Section 15.7(d) of the Collaboration Agreement. A "**Second Tranche Notice**" shall mean an irrevocable written notice specifying a closing date for the purchase of the Second Tranche Shares pursuant to this Section 1.3 (the "**Second Tranche Closing**"), which notice shall be delivered no less than ten (10) Trading Days prior to the date of the Second Tranche Closing. At the Second Tranche Closing, the Company shall instruct the Transfer Agent to register the Second Tranche Shares (as defined below) via book entry against delivery to the Company by Purchaser at or before the Second Tranche Closing of Twenty Five Million Dollars ($25,000,000) (the "**Second Tranche Consideration**"), payable in immediately available funds by wire transfer to an account or accounts designated by the Company. The "**Second Tranche Shares**" shall mean that number of shares of Common Stock equal to Twenty Five Million Dollars ($25,000,000) divided by the Bloomberg volume-weighted average price for a share of Common Stock on the NASDAQ Global Select Market for the 30 Trading Day period ending on the last Trading Day prior to the Second Tranche Notice, rounded to the nearest whole share.

1.4 **Third Tranche Closing.** During the 30 calendar day period following the [***] (as defined in the Collaboration Agreement), the Company shall have the right, but not the obligation, to direct Purchaser, by its delivery to Purchaser of a Third Tranche Notice (as defined below), to purchase the Third Tranche Shares (as defined below) pursuant to this Section 1.4, and Purchaser thereupon shall have the obligation to purchase the Third Tranche Shares, subject to the conditions set forth in this Agreement, provided that the Collaboration Agreement has not been suspended or terminated in accordance with Section 15.7(d) of the Collaboration Agreement. The Company shall notify Purchaser in writing within 5 business days after [***]. A "**Third Tranche Notice**" shall mean an irrevocable written notice specifying a closing date for the purchase of the Third Tranche Shares pursuant to this Section 1.4 (the "**Third Tranche Closing**"), which notice shall be delivered no less than ten (10) Trading Days prior to the date of the Third Tranche Closing. At the Third Tranche Closing, the Company shall instruct the Transfer Agent to register such issuance via book entry the Third Tranche Shares (as defined below) against delivery to the Company by Purchaser at or before the Third Tranche Closing of Ten Million Dollars ($10,000,000) (the "**Third Tranche Consideration**"), payable in immediately available funds by wire transfer to an account or accounts designated by the Company. The "**Third Tranche Shares**" shall mean that number of shares of Common Stock equal to Ten Million Dollars ($10,000,000) divided by the Bloomberg volume-weighted average price for a share of Common Stock on the NASDAQ Global Select Market for the 30 Trading Day period ending on the last Trading Day prior to the Third Tranche Notice, rounded to the nearest whole share. For clarity, each of the Initial Closing, Second Tranche Closing and Third Tranche Closing shall be referred to as a "**Closing**."

1.5 **Capital Adjustments.** If after the date hereof (A) the Company shall pay a dividend in securities of the Company (other than in Common Stock) or of other property (including cash) on the Common Stock, or (B) there shall occur any merger, consolidation, capital reorganization or reclassification in which the Common Stock is converted or exchanged for securities, cash or other property, the class or series of stock constituting the Common Stock for purposes of this Agreement, shall be appropriately adjusted to reflect such other dividend, merger, consolidation, capital reorganization or reclassification. After any event referenced in clauses (A) and (B) of the preceding sentence is consummated, all references herein to the Common Stock shall be deemed to refer to the capital stock or

property (including cash) into or for which the Common Stock was converted or exchanged, with the necessary changes in detail.

2. REPRESENTATIONS AND WARRANTIES OF THE COMPANY

As of the date of each Closing, the Company represents and warrants to Purchaser that, subject to exceptions and disclosures set forth in any part or subpart of the Company Disclosure Schedule corresponding to the particular Section or subsection of this Section 2, or any exceptions or disclosures set forth in any other part or subpart of the Company Disclosure Schedule to the extent it is reasonably apparent from the wording or any such exception or disclosure that such exception or disclosure is applicable to qualify such representation or warranty, and (i) in the case of the Initial Closing, only to the extent specifically referenced in the applicable representation or warranty, disclosures in the SEC Filings (as defined below) and (ii) in the case of the Second Tranche Closing and Third Tranche Closing, disclosures in the SEC Filings, provided that in cases (i) or (ii), in any event excluding any disclosure of risks included in any "risk factors," "forward-looking statements" disclaimer or other statements that are similarly predictive or forward-looking in nature, the statements contained in this Section 2 are true, complete and correct (except that those statements which address matters only as of a particular date are true, correct and complete as of such date). The Company shall deliver an updated and current Company Disclosure Schedule prior to each Closing.

2.1 Organization and Qualification. The Company is a corporation duly organized, validly existing and in good standing under the laws of the State of Delaware and has all requisite corporate power and authority to own, lease and operate its properties and assets and to carry on its business as now conducted and as it is described in the SEC Filings. The Company is duly qualified to transact business and is in good standing in each jurisdiction in which the failure to so qualify would or would be reasonably expected to have, individually or in the aggregate, a material adverse effect on (i) the business, properties or financial condition of the Company, (ii) the Shares or (iii) the enforceability of this Agreement (a "**Material Adverse Effect**"); *provided* that none of the following shall be taken into account in determining whether there is a Material Adverse Effect: (a) any change in the market price or trading volume of the Company's stock; (b) any event, circumstance, change or effect in the industries in which the Company or its subsidiaries operates generally or the United States or European economy generally, financial markets or political conditions generally; (c) any act of terrorism, military action or war (whether or not declared), national or international calamity or similar event or any escalation or worsening thereof; (d) any event, circumstance, change or effect arising from or relating to any change in legal requirements or generally accepted accounting principles ("**GAAP**") (or interpretations of any legal requirements or GAAP); or (e) any change or effect attributable to the consummation of the transactions contemplated hereby, or the public announcement of the execution of, this Agreement (provided any such public announcement is not in breach of this Agreement); *provided*, in each case, that such effects do not, individually or in the aggregate, have a materially disproportionate adverse impact on the Company, taken as a whole, relative to any other "person" as such term is defined under Section 3(a)(9) of the Securities Exchange Act of 1934, as amended (the "**Exchange Act**") and as used in Sections 13(d)(3) and 14(d)(2) of the Exchange Act ("**Person**") in the industries or markets in which the Company operates.

2.2 Certificate of Incorporation and Bylaws. The certificate of incorporation, bylaws and documents of similar substance (the "**Governing Documents**") of the Company and its subsidiaries that are on file with the United States Securities and Exchange Commission (the "**SEC**") are current, complete and correct copies thereof as in effect on the date hereof. The Governing Documents of the Company and its subsidiaries are in full force and effect. The Company and each subsidiary of the Company are in compliance with the terms of their respective Governing Documents.

2.3 Capitalization.

(a) The authorized capital stock of the Company consists of 275,000,000 shares of capital stock, of which 250,000,000 are designated as Common Stock and 25,000,000 are designated as preferred stock, $0.001 par value per share ("**Preferred Stock**"). As of the close of business on the date that is two Trading Days prior to the date of this Agreement, (i) 39,039,083 shares of Common Stock were issued and outstanding, all of which were validly issued and fully paid, nonassessable and free of preemptive rights; (ii) 5,128,090 shares of Common Stock were issuable (and such number was reserved for issuance) upon exercise of options to purchase Common Stock or as restricted stock units payable in Common Stock (the "**Options**") outstanding as of such date; (iii) 149,700 shares of Common Stock were issuable (and such number was reserved for issuance) upon exercise of warrants to purchase Common Stock (the "**Warrants**") outstanding as of such date; and (iv) no shares of Preferred Stock were issued and outstanding.

(b) As of the close of business on the last Trading Day immediately preceding the date of this Agreement, except for (i) the Options and (ii) the Warrants, there were no options, warrants or other rights to acquire capital stock or other equity interests from the Company, or securities convertible into or exchangeable for such capital stock or other equity interests. Other than (A) shares of capital stock reserved for issuance as provided in this Section 2.3 and (B) options to purchase Common Stock or other equity awards issued in accordance with the Company's 2011 Equity Incentive Plan or 2014 Incentive Plan and shares subject to purchase under the 2014 Employee Stock Purchase Plan (collectively, the "**Awards**"), the Company has not issued any shares of its capital stock or other equity interests, or securities convertible into or exchangeable for such capital stock or other equity interests except as set forth in its filings under the Securities Act of 1933, as amended ("**Securities Act**") and the Exchange Act. All outstanding shares of Common Stock and all shares of Common Stock subject to issuance upon exercise of the Options, the Awards and the Warrants, upon issuance prior to the Closing on the terms and conditions specified in the instruments pursuant to which they are issuable, will be duly authorized, validly issued, fully paid, nonassessable and free of preemptive rights. The Shares to be issued in connection with the Agreement, when issued as contemplated herein, will be duly authorized, validly issued, fully paid and nonassessable, will not be in violation of any preemptive rights and will be free and clear of all liens, charges, restrictions, claims, rights of first refusal and encumbrances except as set forth in this Agreement and the Company's Governing Documents. The issuance and sale of the Shares will not obligate the Company to issue shares of Common Stock or other securities to any Person (other than the Purchaser) and will not result in a right of any holder of Company securities to adjust the exercise, conversion, exchange or reset price under any of such securities.

2.4 Authorization; Enforceability.

(a) The Company has all requisite corporate power and authority to execute, deliver and perform, as applicable, this Agreement and to issue and sell the Shares in accordance with the terms hereof.

(b) All corporate action on the part of the Company and its officers and directors necessary for (i) the authorization, execution, delivery and performance of all obligations of the Company under this Agreement has been taken and (ii) the issuance and sale by the Company of the Shares hereunder has been taken. This Agreement constitutes a valid and legally binding obligation of the Company, enforceable in accordance with its terms, except (A) as limited by applicable bankruptcy, insolvency, reorganization, moratorium and other laws of general application affecting enforcement of creditors' rights generally or by equitable principles and (B) as limited by laws relating to the availability of specific performance, injunctive relief or other equitable remedies (the "**Equitable Exceptions**"). No action on the part of the Company's stockholders is necessary for the authorization, execution, delivery or performance of the Company's obligations hereunder.

2.5 SEC Filings; Financial Statements.

(a) The Company has timely filed with or furnished to the SEC all registration statements, prospectuses, forms, reports, definitive proxy statements, schedules and documents required to be filed by it under the Securities Act or the Exchange Act, as the case may be (collectively, the "**SEC Filings**"). Each SEC Filing, as amended or supplemented, if applicable, (i) as of its date, or, if amended, as of the date of the last such amendment, complied in all material respects with the applicable requirements of the Securities Act, the Exchange Act and the Sarbanes-Oxley Act of 2002, as amended (the "**Sarbanes-Oxley Act**"), as the case may be, and the rules and regulations of the SEC thereunder, applicable to such SEC Filing, and (ii) did not, at the time it was filed (or at the time it became effective in the case of registration statements), or, if amended, as of the date of the last such amendment, contain any untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary in order to make the statements made therein, in the light of the circumstances under which they were made, not misleading. The Company has never been an issuer subject to Rule 144(i) under the Securities Act. As of the Initial Closing, the Company meets the "Registrant Requirements" for eligibility to use Form S-3 set forth in General Instruction I.A to Form S-3. As of the date of this Agreement, there are no outstanding or unresolved comments in comment letters received from the SEC staff with respect to the SEC Filings and, to the Company's knowledge, none of the SEC Filings is the subject of ongoing SEC review, outstanding SEC comment or outstanding SEC investigation.

(b) Each of the consolidated financial statements (including, in each case, any notes thereto) contained in the SEC Filings, as amended, supplemented or restated, if applicable, was prepared in accordance with GAAP applied (except as may be indicated in the notes thereto and, in the case of unaudited quarterly financial statements, as permitted by the Form 10-Q under the Exchange Act) on a consistent basis throughout the periods indicated (except as may be indicated in the notes thereto), and each presented fairly, in all material respects, the consolidated financial position, results of operations and cash flows of the Company and the consolidated subsidiaries of the Company as of the respective dates thereof and for the respective periods indicated therein (subject, in the case of unaudited quarterly financial statements, to normal year-end adjustments).

(c) The Company and its subsidiaries have implemented and maintain a system of internal control over financial reporting (as required by Rule 13a-15(a) under the Exchange Act) that is designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of consolidated financial statements in accordance with GAAP for external purposes and includes policies and procedures that (i) pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of the assets of the Company, (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with GAAP and to maintain accountability of assets, and that receipts and expenditures of the Company are being made only in accordance with authorizations of management and directors of the Company, and (iii) provide reasonable assurance regarding the prevention or timely detection of unauthorized acquisition, use or disposition of the Company's assets that could have a material effect on its financial statements, and such system of internal control over financial reporting is reasonably effective.

(d) The Company has implemented and maintains disclosure controls and procedures (as defined in Rule 13a-15(d) of the Exchange Act) that are designed to ensure that information required to be disclosed by the Company in the reports it files or submits under the Exchange Act is recorded, processed, summarized and reported within the time frames specified by the SEC's rules and forms (and such disclosure controls and procedures are reasonably effective), and has disclosed, based on its most recent evaluation of its system of internal control over financial reporting prior to the date of this Agreement, to the Company's independent registered accountant and the audit committee of the Board of

Directors (A) any significant deficiencies and material weaknesses to the Company's Knowledge in the design or operation of its internal control over financial reporting (as defined in Rule 13a-15(f) of the Exchange Act) and (B) to the Company's Knowledge any fraud that involves management or other employees who have a significant role in the Company's internal control over financial reporting.

2.6 **No Conflict; Required Filings and Consents.**

(a) The execution and delivery of this Agreement by the Company does not, and the performance of this Agreement by the Company will not, (i) conflict with or violate any provision of the Governing Documents of the Company or its subsidiaries, (ii) assuming that all consents, approvals, authorizations and permits described in the Collaboration Agreement have been obtained, conflict with or violate any law applicable to the Company or by which any property or asset of the Company is bound or affected or (iii) conflict with, or constitute a default (or an event which, with notice or lapse of time or both, would become a default) under, or give to others any rights of termination, amendment, acceleration or cancellation of, any Material Contract (as defined below).

(b) The Company is not required to obtain any consent, waiver, authorization or order of, give any notice to, or make any filing or registration with, any federal, national, supranational, state, provincial, municipal, local or other government, governmental, regulatory or administrative authority, agency or commission or any court, tribunal, or judicial or arbitral body of competent jurisdiction ("**Governmental Authority**") or other Person in connection with the execution, delivery and performance by the Company of the issuance of the Shares, other than (i) (A) the filing of a prospectus (and potentially the filing of a registration statement) with the SEC in accordance with the requirements of Section 7.2 below, (B) filings required by applicable Blue Sky Laws, (C) the filing of a Notice of Sale of Securities on Form D with the SEC under Regulation D of the Securities Act, (D) the filing of any requisite notices and/or application(s) to the NASDAQ Global Select Market for the issuance and sale of the Shares and the listing of the Shares thereon in the time and manner required thereby, (E) any filing required by the Collaboration Agreement, and (F) those that have been made or obtained prior to the date of this Agreement, or (ii) where failure to obtain such consents, approvals, authorizations or permits, or to make such filings or notifications, would not, individually or in the aggregate, reasonably be expected to have a Material Adverse Effect.

2.7 **Employees and Employee Matters.** Except as would not reasonably be expected to have a Material Adverse Effect, the Company has complied with all federal, state and local laws relating to the hiring of employees, consultants and advisors and the employment of labor, including provisions thereof relating to wages, hours, equal opportunity, collective bargaining and the payment of social security and other taxes. The Company is not delinquent in material payments to any of its employees for any wages, salaries, commissions, bonuses or other direct compensation for any services performed by them to date or amounts required to be reimbursed to such employees or upon any termination of the employment of any such employees.

2.8 **Material Contracts.** Except as disclosed in the SEC Filings, neither the Company nor any of its assets, properties, businesses or operations is a party to, bound or affected by, or receives benefits under any contract which is a "material contract" (as such term is defined in Item 601(b)(10) of Regulation S-K of the SEC) (a "**Material Contract**"). Except as would not, individually or in the aggregate, be reasonably expected to have a Material Adverse Effect, (i) each Material Contract is valid and binding on the Company and, to the Company's knowledge, each other party thereto, and in full force and effect, (ii) each Material Contract is enforceable against the Company and, to the Company's knowledge, the other parties thereto in accordance with the terms thereof, except as such enforceability may be limited by bankruptcy, insolvency, reorganization, moratorium and other similar laws of general applicability relating to or affecting creditor's rights generally and by the application of general principles

of equity and (iii) the Company has not received written notice of any violation or default under (or any condition which with the passage of time or the giving of notice would cause such a violation of or default under) any Material Contract.

2.9 **Litigation.** There is no material action, suit or proceeding pending or, to the Company's knowledge, currently threatened against the Company or against any director, officer or employee of the Company. The Company is not a party to, or subject to the provisions of, any order, writ, injunction, judgment or decree of any court or government agency or instrumentality. There is no material action, suit, proceeding or investigation by the Company currently pending or that the Company intends to initiate.

2.10 **Taxes.** Except as would not reasonably be expected to have a Material Adverse Effect, (i) all federal, state and local tax returns, reports and declarations of the Company required by law to be filed have been duly filed, (ii) all taxes and other fees due thereon have been paid and (iii) the Company has set aside on its books provisions reasonably adequate for the payment of all material taxes for periods subsequent to the periods to which such returns, reports or declarations apply. There is no tax lien, whether imposed by any federal, state, county or local taxing authority, outstanding against the assets, properties or business of the Company. There are no unpaid taxes in any material amount claimed to be due by the taxing authority of any jurisdiction, and the officers of the Company know of no basis for any such claim.

2.11 **Listing and Maintenance Requirements.** The Common Stock is registered pursuant to Section 12(b) or 12(g) of the Exchange Act, and the Company has taken no action designed to, or which to its knowledge is likely to have the effect of, terminating the registration of the Common Stock under the Exchange Act nor has the Company received any notification that the Commission is contemplating terminating such registration. The Company is in compliance with the requirements of the NASDAQ Global Select Market for continued listing of the Common Stock thereon and has not received any notification that the NASDAQ Global Select Market is contemplating terminating such listing. The Company has no reason to believe that it will not upon issuance of the Shares continue to be in compliance with all such listing and maintenance requirements. The issuance of the Shares hereunder does not contravene the rules of the NASDAQ Global Select Market.

2.12 **Offering Exemption.** Based in part on the representations of Purchaser set forth in Section 4.2 below, the offer, sale and issuance of the Shares in conformity with the terms of this Agreement are exempt from the registration requirements of the Securities Act and are exempt from the qualification or registration requirements of applicable state securities laws. Neither the Company nor its affiliates, nor any agent on its or their behalf, (i) has engaged in any form of general solicitation or general advertising (within the meaning of Regulation D under the Securities Act) in connection with the Common Stock Financing, (ii) has solicited or will solicit any offers to sell or has offered to sell or will offer to sell all or any part of the Shares to any Person or Persons so as to bring the sale of the Shares by the Company within the registration provisions of the Securities Act or any state securities laws or (iii) has issued any shares of Common Stock or shares of any series of Preferred Stock or other securities or instruments convertible into, exchangeable for or otherwise entitling the holder thereof to acquire shares of Common Stock which would be integrated with the sale of the Shares to Purchaser for purposes of the Securities Act or of any applicable shareholder approval provisions, including, without limitation, under the rules and regulations of any exchange or automated quotation system on which any of the securities of the Company are listed or designated, nor will the Company or any of its subsidiaries or affiliates take any action or steps that would require registration of any of the Shares under the Securities Act.

2.13 **Affiliate Transactions.** No employee, officer, director or 10% or greater shareholder of the Company or member of his or her immediate family (each a "**Covered Person**") is currently indebted

to the Company, nor is the Company indebted (or committed to make loans or extend or guarantee credit) to any Covered Person. Except as disclosed in the SEC Filings, as of the date hereof, no Covered Person has any direct or indirect ownership interest in any firm or corporation with which the Company is affiliated or with which the Company has a business relationship, or any firm or corporation that competes with the Company (except for ownership of stock not to exceed 1% of the outstanding capital stock of any publicly traded company that may compete with the Company).

2.14 **Investment Company Act.** The Company is not, and is not an Affiliate (as defined below) of, and after giving effect to the Common Stock Financing, will not be and will not be an Affiliate of, an "investment company" or an entity "controlled" by an "investment company," as such terms are defined in the Investment Company Act of 1940. For purposes of this Agreement, "**Affiliate**" shall mean any Person that, directly or indirectly through one or more intermediaries, controls or is controlled by or is under common control with a Person, as such terms are used in and construed under Rule 405 under the Securities Act.

2.15 **Brokers or Finders.** The Company has not retained any brokers, consultants or advisors in connection with this Agreement, and has no agreements to pay any commission or compensation in the nature of a finder's or broker's fee arising out of this Agreement or the transactions contemplated hereby.

2.16 **Compliance with Rule 506.** None of the Company, any of its predecessors, any affiliated issuer, any director, executive officer, other officer of the Company participating in the offering contemplated hereby, any beneficial owner of 20% or more of the Company's outstanding voting equity securities, calculated on the basis of voting power, nor any promoter (as that term is defined in Rule 405 under the Securities Act) connected with the Company in any capacity at the time of sale is disqualified from relying on Rule 506 of Regulation D under the Securities Act ("**Rule 506**") for any of the reasons stated in Rule 506(d) in connection with the issuance and sale of the Shares to Purchaser pursuant to this Agreement. The Company has exercised reasonable care, including without limitation, conducting a factual inquiry that is appropriate in light of the circumstances, into whether any such disqualification under Rule 506(d) exists, but has assumed the accuracy of the Purchaser's representations and warranties. The Company has furnished to Purchaser, a reasonable time prior to the date hereof, a description in writing of any matters that would have triggered disqualification under Rule 506(d) but which occurred before September 23, 2013, in each case, in compliance with the disclosure requirements of Rule 506(e). The Company has exercised reasonable care, including without limitation, conducting a factual inquiry that is appropriate in light of the circumstances, into whether any such disqualification under Rule 506(d) would have existed and whether any disclosure is required to be made to Purchaser under Rule 506(e). Any outstanding securities of the Company (of any kind or nature) that were issued in reliance on Rule 506 at any time on or after September 23, 2013 have been issued in compliance with Rules 506(d) and (e) and no party has any reasonable basis for challenging any such reliance on Rule 506 in connection therewith.

3. ADDITIONAL REPRESENTATIONS AND WARRANTIES OF THE COMPANY AS OF THE INITIAL CLOSING

As of the date of the Initial Closing only, the Company represents and warrants to Purchaser that, subject to exceptions and disclosures set forth in any part or subpart of the Company Disclosure Schedule corresponding to the particular Section or subsection of this Section 3, or any exceptions or disclosures set forth in any other part or subpart of the Company Disclosure Schedule to the extent it is reasonably apparent from the wording or any such exception or disclosure that such exception or disclosure is applicable to qualify such representation or warranty, and disclosures in the SEC Filings, excluding any disclosure of risks included in any "risk factors," "forward-looking statements" disclaimer or other statements that are similarly predictive or forward-looking in nature, the statements contained in this

Section 3 are true, complete and correct (except that those statements which address matters only as of a particular date are true, correct and complete as of such date).

3.1 **Material Changes; Undisclosed Events, Liabilities or Developments.** Since the date of the latest audited financial statements included within the SEC Filings, except as specifically set forth in a subsequent SEC Filing filed at least one (1) Trading Day prior to the date hereof: (i) there has been no event, occurrence or development that has had or that could reasonably be expected to result in a Material Adverse Effect, (ii) the Company has not incurred any liabilities (contingent or otherwise) other than (a) trade payables and accrued expenses incurred in the ordinary course of business consistent with past practice and (b) liabilities not required to be reflected in the Company's financial statements pursuant to GAAP or disclosed in filings made with the Commission, (iii) the Company has not altered its method of accounting, (iv) the Company has not declared or made any dividend or distribution of cash or other property to the holders of its Common Stock or purchased, redeemed or made any agreements to purchase or redeem any shares of its capital stock and (v) the Company has not issued any equity securities to any officer, director or Affiliate, except pursuant to existing Company stock option plans. The Company does not have pending before the SEC any request for confidential treatment of information. Except for the issuance of the Shares contemplated by this Agreement, no event, liability, fact, circumstance, occurrence or development has occurred or exists or is reasonably expected to occur or exist with respect to the Company or its business, properties, operations, assets or financial condition, that would be required to be disclosed by the Company under applicable securities laws if the Company were publicly offering securities pursuant to an effective registration statement under the Securities Act at the time this representation is made or deemed made that has not been publicly disclosed at least one (1) Trading Day prior to the date that this representation is made.

3.2 **Labor Relations.** No material labor dispute exists or, to the knowledge of the Company, is imminent with respect to any of the employees of the Company, which could reasonably be expected to result in a Material Adverse Effect. None of the Company's employees is a member of a union that relates to such employee's relationship with the Company, the Company is not a party to any collective bargaining agreement, and the Company believes that its relationships with its employees are good. The Company is in compliance with all U.S. federal, state, local and foreign laws and regulations relating to employment and employment practices, terms and conditions of employment and wages and hours, except where the failure to be in compliance could not, individually or in the aggregate, reasonably be expected to have a Material Adverse Effect.

3.3 **Environmental Matters.** The Company is in compliance with and has not received notice of any actual or potential liability under or relating to, or actual or potential violation of, applicable federal, state and local laws, rules and regulations relating to the use, treatment, storage and disposal of hazardous or toxic substances or waste and protection of health and safety or the environment which are applicable to its business (the "**Environmental Laws**"). The Company has not received notice of any actual or potential liability under or relating to, or actual or potential violation of, any Environmental Laws, including for the investigation or remediation of any release or threat of release of hazardous materials, and has no knowledge of any event or condition that would reasonably be expected to result in any such notice. The Company is not conducting or paying for, in whole or in part, any investigation, remediation or other corrective action pursuant to any Environmental Law at any location, and is not a party to any order, decree or agreement that imposes any obligation or liability under any Environmental Law. There are no costs or liabilities associated with Environmental Laws of or relating to the Company, except for any such matter, as would not, individually or in the aggregate, reasonably be expected to have a Material Adverse Effect. The Company is not aware of any facts or issues regarding its compliance with Environmental Laws, or liabilities or other obligations under Environmental Laws, that, individually or in the aggregate, would reasonably be expected to have a Material Adverse Effect, and the Company does not anticipate material capital expenditures relating to any Environmental Laws.

3.4 **Title to Assets.** Except as set forth in the SEC Filings, the Company has good and marketable title in all personal property owned by the Company that is material to the business of the Company, in each case free and clear of all liens, except for liens as do not materially affect the value of such property and do not materially interfere with the use made and proposed to be made of such property by the Company and liens for the payment of federal, state or other taxes, the payment of which is neither delinquent nor subject to penalties. Any real property and facilities held under lease by the Company are held by it under valid, subsisting and enforceable leases with which the Company are in compliance.

3.5 **Insurance.** The Company is insured by insurers of recognized financial responsibility against such losses and risks and in such amounts as are prudent and customary in the business in which the Company is engaged, including, but not limited to, directors and officers insurance. The Company does not have any reason to believe that it will not be able to renew its existing insurance coverage as and when such coverage expires or to obtain similar coverage from similar insurers as may be necessary to continue its business without a significant increase in cost.

3.6 **Registration Rights.** Except as provided for in this Agreement or as set forth in the SEC Filings, no Person has any right to cause the Company to effect the registration under the Securities Act of any securities of the Company.

3.7 **Application of Takeover Protections.** The Company and the Board of Directors have taken all necessary action, if any, in order to render inapplicable any control share acquisition, business combination, poison pill (including any distribution under a rights agreement) or other similar anti- takeover provision under the Company's certificate of incorporation or the laws of its state of incorporation that is or could become applicable to Purchaser as a result of Purchaser and the Company fulfilling their obligations or exercising their rights under this Agreement, including without limitation as a result of the Company's issuance of the Shares and the Purchaser's ownership of the Shares.

3.8 **Foreign Corrupt Practices.** Neither the Company, nor to the knowledge of the Company, any agent or other person acting on behalf of the Company, has: (i) directly or indirectly, used any funds for unlawful contributions, gifts, entertainment or other unlawful expenses related to foreign or domestic political activity, (ii) made any unlawful payment to foreign or domestic government officials or employees or to any foreign or domestic political parties or campaigns from corporate funds, (iii) failed to disclose fully any contribution made by the Company (or made by any person acting on its behalf of which the Company is aware) which is in violation of law or (iv) violated in any material respect any provision of the Foreign Corrupt Practices Act of 1977, as amended.

3.9 **Accountants.** The Company's independent registered public accounting firm is Ernst & Young LLP. To the knowledge and belief of the Company, such accounting firm: (i) is a registered public accounting firm as required by the Exchange Act and (ii) shall express its opinion with respect to the financial statements to be included in the Company's Annual Report for the fiscal year ending December 31, 2016.

3.10 **Office of Foreign Assets Control.** Neither the Company nor, to the Company's knowledge, any director, officer, agent, employee or Person acting on behalf of the Company, is currently subject to any U.S. sanctions administered by the Office of Foreign Assets Control of the U.S. Treasury Department.

3.11 **Money Laundering.** The operations of the Company are and have been conducted at all times in compliance with applicable financial record-keeping and reporting requirements of the Currency and Foreign Transactions Reporting Act of 1970, as amended, applicable money laundering statutes and applicable rules and regulations thereunder (collectively, the "**Money Laundering Laws**"), and no

action, suit or proceeding by or before any court or governmental agency, authority or body or any arbitrator involving the Company with respect to the Money Laundering Laws is pending or, to the knowledge of the Company, threatened.

3.12 **Acknowledgement.** The Company acknowledges and agrees that Purchaser is acting solely in the capacity of an arm's length purchaser with respect to this Agreement and the transactions contemplated hereby. The Company further acknowledges that Purchaser is not acting as a financial advisor or fiduciary of the Company (or in any similar capacity) with respect to this Agreement and the transactions contemplated hereby and any advice given by Purchaser or any of their respective representatives or agents in connection with this Agreement and the transactions contemplated hereby is merely incidental to Purchaser's purchase of the Shares. The Company further represents to Purchaser that the Company's decision to enter into this Agreement has been based solely on the independent evaluation of the transactions contemplated hereby by the Company and its representatives.

4. REPRESENTATIONS AND WARRANTIES OF PURCHASER

As a material inducement to the Company to enter into and perform its obligations under this Agreement, Purchaser represents and warrants to the Company as follows:

4.1 **Authorization; Enforceability.** Purchaser has all requisite power and authority to execute, deliver and perform this Agreement. All action on the part of Purchaser and, as applicable, its directors, officers, members, partners and shareholders, necessary for the authorization, execution, delivery and performance of all obligations of Purchaser under this Agreement has been taken. This Agreement constitutes the valid and legally binding obligations of Purchaser, enforceable in accordance with their terms, except as limited by the Equitable Exceptions.

4.2 **Investor Representations.**

(a) The Shares acquired by Purchaser hereunder will be acquired by Purchaser for its own account for investment purposes and not with a view to distribution in violation of the Securities Act. Purchaser does not presently have any contract, undertaking or agreement with any Person to sell, transfer or grant participation rights to such Person or to any other Person with respect to any of the Shares acquired by Purchaser hereunder.

(b) Purchaser is an "accredited investor" within the meaning of Rule 501(a) promulgated under the Securities Act.

(c) Purchaser understands that the Shares are characterized as "restricted securities" under the federal securities laws inasmuch as they are being acquired from the Company in a transaction not involving a public offering and that under such laws and applicable regulations such securities may be resold without registration under the Securities Act only in certain limited circumstances. Purchaser acknowledges and agrees that the Shares must be held indefinitely unless they are subsequently registered under the Securities Act or an exemption from such registration is available or the Company receives an opinion of counsel reasonably satisfactory to the Company that such registration is not required. Purchaser has been advised or is aware of the provisions of Rule 144 promulgated under the Securities Act as in effect from time to time ("**Rule 144**"), which permit limited resale of shares purchased in a private placement subject to the satisfaction of certain conditions.

(d) Purchaser acknowledges and agrees that it can bear the economic risk of its investment in the Shares and has such knowledge and experience in financial or business matters that it is capable of evaluating the merits and risks of the investment in the Shares. Purchaser believes that it has

received all the information it considers necessary or appropriate for deciding whether to purchase the Shares acquired by Purchaser hereunder. Purchaser further represents that it has had an opportunity to ask questions and receive answers from the Company regarding the terms and conditions of the offering of the Shares.

(e) Purchaser has not agreed to incur, directly or indirectly, any liability for brokerage or finders' fees, agents' commissions or other similar charges in connection with this Agreement or any of the transactions contemplated hereby.

(f) Purchaser is not relying and has not relied on any representations or warranties whatsoever regarding the subject matter of this Agreement, express or implied, except for the representations and warranties in Section 2 and Section 3, including the Company Disclosure Schedule. Such representations and warranties by the Company constitute the sole and exclusive representations and warranties of the Company in connection with the transactions contemplated by this Agreement and Purchaser understands, acknowledges and agrees that all other representations and warranties of any kind or nature whether express, implied or statutory are specifically disclaimed by the Company.

(g) In connection with the due diligence investigation of the Company by Purchaser and its affiliates, stockholders, directors, officers, employees, agents, representatives or advisors, Purchaser and its affiliates, stockholders, directors, officers, employees, agents, representatives and advisors have received and may continue to receive after the date hereof from the Company and its affiliates, stockholders, directors, officers, employees, consultants, agents, representatives and advisors certain estimates, projections, forecasts and other forward-looking information, as well as certain business plan information, regarding the Company and its business and operations. Purchaser hereby acknowledges that there are uncertainties inherent in attempting to make such estimates, projections, forecasts and other forward-looking statements, as well as in such business plans, and that Purchaser will have no claim against the Company, or any of its affiliates, stockholders, directors, officers, employees, consultants, agents, representatives or advisors, or any other Person with respect thereto unless any such information is expressly addressed or included in a representation or warranty contained in this Agreement. Accordingly, Purchaser hereby acknowledges and agrees that neither the Company nor any of its respective affiliates, stockholders, directors, officers, employees, consultants, agents, representatives or advisors, nor any other Person, has made or is making any express or implied representation or warranty with respect to such estimates, projections, forecasts, forward-looking statements or business plans unless any such information is expressly addressed or included in a representation or warranty contained in this Agreement.

4.3 Compliance with Laws. Neither Purchaser nor, to Purchaser's knowledge, any director, officer, agent, employee or Person acting on behalf of Purchaser, is currently subject to any U.S. sanctions administered by the Office of Foreign Assets Control of the U.S. Treasury Department. Purchaser represents and warrants to the Company as of each Closing as follows: if Purchaser is not a United States person (as defined by Section 7701(a)(30) of the Code), Purchaser has satisfied itself as to the full observance of the laws of its jurisdiction in connection with any invitation to subscribe for the Shares or any use of this Agreement, including (i) the legal requirements within its jurisdiction for the purchase of the Shares, (ii) any foreign exchange restrictions applicable to such purchase, (iii) any governmental or other consents that may need to be obtained and (iv) the income tax and other tax consequences, if any, that may be relevant to the purchase, holding, redemption, sale or transfer of the Shares. Purchaser's subscription and payment for and continued beneficial ownership of the Shares will not violate any applicable securities or other laws of Purchaser's jurisdiction.

5. CONDITIONS TO PURCHASER'S OBLIGATIONS AT CLOSING

The obligations of Purchaser under this Agreement to purchase and pay for the Shares being purchased by Purchaser at each Closing are subject to the satisfaction or waiver, at or prior to the applicable Closing, of the following conditions:

5.1 **Representations and Warranties.** The representations and warranties of the Company contained in Section 2 and Section 3 of this Agreement and in Section 13.1 and Section 13.3 of the Collaboration Agreement shall be true, correct and complete on and as of the Initial Closing and the representations and warranties contained in Section 2 shall be true, correct and complete as of the Second Tranche Closing and Third Tranche Closing (except that those representations and warranties which address matters only as of a particular date need only be measured as of the specific date) except that any inaccuracies in such representations and warranties will be disregarded if they collectively do not constitute and would not reasonably be expected to have a Material Adverse Effect on the Company (it being understood that for purposes of determining the accuracy of any representation or warranties all Material Adverse Effect and other materiality qualifications contained in such representations and warranties will be disregarded).

5.2 **Performance.** The Company shall have performed and complied in all material respects with all other conditions, covenants and agreements contained in this Agreement required to be performed or complied with by it on or before the applicable Closing.

5.3 **Legal Investment.** On the date of the applicable Closing, the sale and issuance of the Shares shall be legally permitted by all laws and regulations to which Purchaser and the Company are subject.

5.4 **No Suspension.** Trading in the Common Stock shall not have been suspended by the SEC or the NASDAQ Global Select Market.

5.5 **Consents and Approvals.** Any consent required for the consummation of the transactions contemplated by this Agreement, including without limitation, the issuance of the Shares, shall have been obtained (collectively, "**Consents**"). If applicable, the waiting period (or any extension thereof) under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended, required in order for the Collaboration Agreement to become effective shall have expired or been terminated.

5.6 **Qualifications.** All authorizations, approvals or permits, if any, of any Governmental Authority that are required in connection with the lawful issuance and sale of the Shares pursuant to this Agreement shall have been duly obtained and shall be effective on and as of the applicable Closing.

5.7 **No Injunction.** No statute, rule, regulation, executive order, decree, ruling or injunction shall have been enacted, entered, promulgated or endorsed by any Governmental Authority of competent jurisdiction which prohibits the consummation of any of the transactions contemplated by this Agreement.

5.8 **Collaboration Agreement.** The Company shall have executed the Collaboration Agreement and the Effective Date of the Collaboration Agreement shall have occurred.

5.9 **Legal Opinion.** Purchaser shall have received from Cooley LLP, counsel for the Company, an opinion, dated as of the Initial Closing, in form and substance reasonably satisfactory to counsel for Purchaser.

5.10 **Compliance Certificate.** Purchaser shall have received a compliance certificate, executed by the Chief Executive Officer and Chief Financial Officer of the Company, dated as of the date of the Closing, to the effect that the conditions specified in Sections 5.1 and 5.2 have been satisfied.

5.11 **Secretary's Certificate .** Purchaser shall have received a certificate of the Company's Secretary certifying as to (A) the Company's certificate of incorporation and bylaws, (B) the resolutions of the Board of Directors approving this Agreement and the transactions contemplated hereby, and (C) good standing certificates with respect to the Company from the applicable authority(ies) in Delaware and any other jurisdiction in which the Company is qualified to do business, dated a recent date before the Closing.

6. CONDITIONS TO THE COMPANY'S OBLIGATIONS AT CLOSING

The obligations of the Company under this Agreement to sell and issue to Purchaser the Shares to be purchased by Purchaser at each Closing are subject to the satisfaction or waiver, at or prior to the applicable Closing, of the following conditions:

6.1 **Representations and Warranties.** The representations and warranties of Purchaser contained in Section 4 shall be true, correct and complete in all respects on and as of the applicable Closing with the same force and effect as if they had been made at such time (except that those representations and warranties which address matters only as of a particular date need only be true, correct and complete in all material respects as of such date).

6.2 **Performance.** Purchaser shall have performed and complied with all other conditions, covenants and agreements contained in this Agreement required to be performed or complied with by Purchaser on or before the applicable Closing.

6.3 **Qualifications.** All authorizations, approvals or permits, if any, of any Governmental Authority that are required in connection with the lawful issuance and sale of the Shares pursuant to this Agreement shall have been duly obtained and shall be effective on and as of the applicable Closing.

6.4 **No Injunction.** No statute, rule, regulation, executive order, decree, ruling or injunction shall have been enacted, entered, promulgated or endorsed by any Governmental Authority of competent jurisdiction which prohibits the consummation of any of the transactions contemplated by this Agreement.

6.5 **Consents and Approvals.** Any Consent required for the consummation of the transactions contemplated by this Agreement, including without limitation, the issuance of the Shares, shall have been obtained. If applicable, the waiting period (or any extension thereof) under the Hart- Scott-Rodino Antitrust Improvements Act of 1976, as amended, required in order for the Collaboration Agreement to become effective shall have expired or been terminated.

6.6 **Collaboration Agreement.** The Company shall have executed the Collaboration Agreement and the Effective Date of the Collaboration Agreement shall have occurred.

7. COVENANTS

7.1 **Purchaser Lock-Up.** Purchaser covenants and agrees as follows:

(a) Purchaser will not, without the prior written consent of the Company, during the period commencing on the date of each Closing and, subject to the terms set forth herein, ending (i) 180

days after the Initial Closing with respect to the Shares purchased in the Initial Closing, or (ii) 90 days after the Second Tranche Closing or Third Tranche Closing, as applicable with respect to the Shares purchased in such Closing (each, a "**Lock-Up Period**"), (i) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend or otherwise transfer or dispose of, directly or indirectly, any Shares purchased in such Closing or (ii) enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of the Shares, whether any such transaction described in clause (i) or (ii) above is to be settled by delivery of the Shares purchased in such Closing, in cash or otherwise. Notwithstanding the foregoing, Purchaser may transfer the Shares to any of its shareholders or Affiliates; *provided* that in the case of any transfer or distribution pursuant to this subparagraph during the Lock-Up Period, each donee or transferee shall sign and deliver a lock-up letter with terms substantially similar to the terms of this Section 7.1.

(b) Notwithstanding anything to the contrary contained herein, Purchaser agrees that Purchaser shall not effect any sale, transfer or other disposition of any Shares unless: (a) such sale, transfer or other disposition is effected pursuant to an effective registration statement under the Securities Act; (b) such sale, transfer or other disposition is made in conformity with the requirements of Rule 144, as evidenced by a broker's letter and a representation letter executed by Purchaser (reasonably satisfactory in form and content to the Company) stating that such requirements have been met; or (c) counsel reasonably satisfactory to the Company (which may be counsel to the Company) shall have advised the Company in a written opinion letter (reasonably satisfactory in form and content to the Company), upon which the Company may rely, that such sale, transfer or other disposition will be exempt from the registration requirements of the Securities Act.

(c) Notwithstanding any other provision of this Section 7.1, this Section 7.1 shall not prohibit or restrict any disposition of Common Stock by Purchaser in connection with (i) a bona fide tender offer by a Person other than Purchaser or the Company that is not opposed by the Board of Directors and involving a Change of Control of the Company (as defined below); or (ii) an issuer tender offer by the Company; *provided*, that in the event that the tender offer is not completed, the Shares shall remain subject to the restrictions contained in this Section 7.1. For the purposes of this Agreement, a "**Change of Control**" means the transfer, in one transaction or a series of related transactions, to a person or group of affiliated persons, of shares of capital stock of the Company if, after such transfer, the stockholders of the Company immediately prior to such transfer do not own at least twenty percent (20%) of the outstanding voting securities of the Company (or the surviving entity).

(d) Purchaser acknowledges and agrees that stop transfer instructions will be given to the Company's transfer agent with respect to the Shares until the expiration of the Lock-Up Period.

7.2 **Registration Rights.** The Company covenants and agrees as follows:

(a) As soon as practicable, and in any event within thirty (30) days following the Initial Closing, the Company shall register the Shares purchased at the Initial Closing on an active Form S-3 or file a new Form S-3 registration statement (or such other form appropriate for such purpose) under the Securities Act. For each Additional Closing, if at any time when it is eligible to use a Form S-3 registration statement, the Company shall as soon as practicable, and in any event within thirty (30) days after the date of purchase by Purchaser, either register on an active Form S-3 or file a new Form S-3 registration statement (or such other form appropriate for such purpose) under the Securities Act covering all Registrable Shares (as defined below) then purchased by Purchaser (and, at the discretion of the Company, other registrable shares held by other shareholders), subject to the limitations of Sections 7.2(b) and 7.2(c). The Company shall maintain the effectiveness of any registration statements with respect to the Registrable Shares in accordance with the terms hereof for a period ending on the date on

which all Registrable Shares covered by such registration statement have been sold pursuant to such registration statement or have otherwise ceased to be Registrable Shares. The Company and the Purchaser agree that the Purchaser will suffer damages if the Company fails to fulfill its obligations under this Section 7.2(a) and that it would not be feasible to ascertain the extent of such damages with precision. Accordingly, if: (i) a registration statement is not filed with the Commission within the time period contemplated hereby; or (ii) a registration statement is not declared effective by the Commission within the time period contemplated hereby (each such event referred to in the foregoing clauses (i) and (ii), a "**Registration Default**"), then in such event as relief for the damages to Purchaser for the Registration Default, and not as a penalty, the Company hereby agrees to pay to Purchaser, an amount in cash equal to 1.0% of the aggregate purchase price of the unregistered Registrable Shares held by Purchaser for each 30-day period (prorated for periods totaling less than 30 days) following the Registration Default until the earlier to occur of: (1) such time as when the Company cures the Registration Default; and (2) the six (6) month anniversary of the applicable Closing Date. The payments to which a Holder shall be entitled pursuant to this Section 7.2(a) are referred to herein as "**Additional Payment Amounts**". The Company shall pay Additional Payment Amounts, if any, to Holders on the earlier of: (1) the last day of the calendar month during which such Additional Payment Amounts are incurred; and (2) the third Business Day following the date on which the Registration Default giving rise to the Additional Payment Amounts is cured.

(b) Notwithstanding the foregoing obligations, if the Company furnishes to Purchaser a certificate signed by the Company's Chief Executive Officer stating that in the good faith judgment of the Board of Directors it would be materially detrimental to the Company and its shareholders for a registration statement with respect to Registrable Shares to either become effective or remain effective for as long as such registration statement otherwise would be required to remain effective, because such action would (i) materially interfere with a significant acquisition, corporate reorganization or other similar transaction involving the Company; (ii) require premature disclosure of material information that the Company has a *bona fide* business purpose for preserving as confidential; or (iii) render the Company unable to comply with requirements under the Securities Act or Exchange Act, then the Company shall have the right to defer taking action with respect to such filing, and any time periods with respect to filing or effectiveness thereof shall be tolled correspondingly, for a period not to exceed 60 days after the applicable Closing Date for the purchase of such Registrable Shares; *provided*, that the Company may not invoke this right more than once in any twelve (12) month period.

(c) The Company shall not be obligated to effect, or to take any action to effect, any registration pursuant to Section 7.2(a) during the period that is 30 days before the Company's good faith estimate of the date of filing with the SEC of, and ending on a date that is 90 days after the effective date of, a Company-initiated registration statement pertaining to an underwritten public offering for the Company's account, *provided* that the Company is actively employing in good faith commercially reasonable efforts to cause such registration statement to become effective; *provided*, *however*, that a "Company-initiated registration statement" shall not include a registration statement on Forms S-4 or S-8 (or any similar or successor form providing for the registration of securities in connection with mergers, acquisitions, exchange offers, subscription offers, dividend reinvestment plans or stock option or other executive or employee benefit or compensation plans). A registration shall not be counted as "effected" for purposes of this Section 7.2(c) until such time as the applicable registration statement has been declared effective by the SEC, unless Purchaser withdraws its request for such registration, in which case such withdrawn registration statement shall be counted as "effected" for purposes of this Section 7.2(c).

(d) All expenses, other than Selling Expenses (as defined below), incurred in connection with registrations, filings or qualifications pursuant to this Section 7.2, including all registration, filing and qualification fees; printers' and accounting fees; fees and disbursements of counsel for the Company; and the reasonable fees and disbursements, shall be borne and paid by the Company.

All Selling Expenses shall be borne by the Purchaser; or if there are other selling shareholders with shares being registered pursuant to such registration statement, then *pro rata* by the selling shareholders based on the number of shares sold by such selling shareholder in the offering.

(e) For the purposes of this Section 7.2,

(i) "**Losses**" means any loss, damage, claim or liability (joint or several) to which a party hereto may become subject under the Securities Act, the Exchange Act, or other federal or state law, insofar as such loss, damage, claim or liability (or any action in respect thereof) arises out of or is based upon: (i) any untrue statement or alleged untrue statement of a material fact contained in any registration statement of the Company, including any preliminary prospectus or final prospectus contained therein or any amendments or supplements thereto; (ii) an omission or alleged omission to state therein a material fact required to be stated therein, or necessary to make the statements therein not misleading; or (iii) any violation or alleged violation by the indemnifying party (or any of its agents or Affiliates) of the Securities Act, the Exchange Act, any state securities law, or any rule or regulation promulgated under the Securities Act, the Exchange Act, or any state securities law.

(ii) "**Registrable Shares**" means the Shares held by Purchaser including, without limitation, any shares of Common Stock paid, issued or distributed in respect of any such Shares by way of stock dividend, stock split or distribution, or in connection with a combination of shares, recapitalization, reorganization, merger or consolidation, or otherwise, but excluding shares of Common Stock acquired in the open market before or after the date hereof, *provided*, *however*, that the Shares will cease to be "Registrable Shares" when (A) the Shares have been sold pursuant to an effective registration statement or (B) the Shares proposed to be sold by Purchaser, in the opinion of counsel satisfactory to the Company, may be distributed to the public without any limitation pursuant to Rule 144 (or any successor provision then in effect).

(iii) "Selling Expenses" means the fees and disbursements of counsel for Purchaser.

(f) With a view to making available to Purchaser the benefits of Rule 144, for a period of one year following the date of the latest Closing pursuant to this Agreement, the Company covenants that it will (i) use its commercially reasonable efforts to file in a timely manner all reports and other documents required, if any, to be filed by it under the Securities Act and the Exchange Act and the rules and regulations adopted thereunder and (ii) make available information necessary to comply with Rule 144 with respect to resales of the Registrable Shares under the Securities Act, at all times, all to the extent required from time to time to enable Purchaser to sell Registrable Shares without registration under the Securities Act within the limitation of the exemptions provided by (A) Rule 144 (if available with respect to resales of the Registrable Shares), as such rule may be amended from time to time or (B) any other rules or regulations now existing or hereafter adopted by the SEC.

(g) To the extent permitted by law, the Company will indemnify and hold harmless Purchaser, and the partners, members, officers, directors, and stockholders of Purchaser; legal counsel and accountants for Purchaser; any underwriter (as defined in the Securities Act) for Purchaser; and each Person, if any, who controls Purchaser or underwriter within the meaning of the Securities Act or the Exchange Act, against any Losses, and the Company will pay to Purchaser, underwriter, controlling Person, or other aforementioned Person any legal or other expenses reasonably incurred thereby in connection with investigating or defending any claim or proceeding from which Losses may result, as such expenses are incurred; *provided*, *however*, that the indemnity agreement contained in this Section 7.2(g) shall not apply to amounts paid in settlement of any such claim or proceeding if such settlement is effected without the consent of the Company, which consent shall not be unreasonably withheld, nor shall

the Company be liable for any Losses to the extent that they arise out of or are based upon actions or omissions made in reliance upon and in conformity with written information furnished by or on behalf of any the Purchaser, underwriter, controlling Person, or other aforementioned Person expressly for use in connection with such registration.

(h) To the extent permitted by law, Purchaser agrees to indemnify and hold harmless the Company, each of the directors of the Company, each of the officers of the Company who shall have signed a registration statement, and each other Person, if any, who controls the Company within the meaning of the Securities Act or the Exchange Act, against any Losses to which they or any of them may become subject under the Securities Act, the Exchange Act or otherwise, insofar as such Losses (or actions in respect thereof) arise out of or are based upon any untrue statement or alleged untrue statement of a material fact contained in a registration statement or any document incorporated by reference in such document, or arise out of or are based upon the omission or alleged omission to state therein a material fact required to be stated therein or necessary to make the statements therein, in light of the circumstances under which they were made, not misleading, in each case to the extent, but only to the extent, that any such Loss arises out of or is based upon any such untrue statement or alleged untrue statement or omission or alleged omission made therein in reliance upon and in strict conformity with written information furnished to the Company by or on behalf of Purchaser for use therein; *provided*, *however*, that the indemnity agreement contained in this Section 7.2(h) shall not apply to amounts paid in settlement of any such claim or proceeding if such settlement is effected without the consent of the Purchaser, which consent shall not be unreasonably withheld;. The maximum aggregate amount of indemnifiable Losses that may be recovered from the Purchaser under the provisions of this Section 7.2(h) shall be the aggregate value of the consideration received for the Shares.

(i) Promptly after receipt by an indemnified party under this Section 7.2 of notice of the commencement of any action (including any governmental action) for which a party may be entitled to indemnification hereunder, such indemnified party will, if a claim in respect thereof is to be made against any indemnifying party under this Section 7.2, give the indemnifying party notice of the commencement thereof. The indemnifying party shall have the right to participate in such action and, to the extent the indemnifying party so desires, participate jointly with any other indemnifying party to which notice has been given, and to assume the defense thereof with counsel mutually satisfactory to the parties; *provided*, *however*, that an indemnified party (together with all other indemnified parties that may be represented without conflict by one counsel) shall have the right to retain one separate counsel, with the fees and expenses to be paid by the indemnifying party, if representation of such indemnified party by the counsel retained by the indemnifying party would be inappropriate due to actual or potential differing interests between such indemnified party and any other party represented by such counsel in such action. The failure to give notice to the indemnifying party within a reasonable time of the commencement of any such action shall relieve such indemnifying party of any liability to the indemnified party under this Section 7.2, to the extent that such failure materially prejudices the indemnifying party's ability to defend such action. The failure to give notice to the indemnifying party will not relieve it of any liability that it may have to any indemnified party otherwise than under this Section 7.2.

(j) To provide for just and equitable contribution to joint liability under the Securities Act in any case in which either: (i) any party otherwise entitled to indemnification hereunder makes a claim for indemnification pursuant to this Section 7.2 but it is judicially determined (by the entry of a final judgment or decree by a court of competent jurisdiction and the expiration of time to appeal or the denial of the last right of appeal) that such indemnification may not be enforced in such case, notwithstanding the fact that this Section 7.2 provides for indemnification in such case, or (ii) contribution under the Securities Act may be required on the part of any party hereto for which indemnification is provided under this Section 7.2, then, and in each such case, such parties will contribute to the aggregate losses, claims, damages, liabilities, or expenses to which they may be subject

(after contribution from others) in such proportion as is appropriate to reflect the relative fault of each of the indemnifying party and the indemnified party in connection with the statements, omissions, or other actions that resulted in such loss, claim, damage, liability, or expense, as well as to reflect any other relevant equitable considerations. The relative fault of the indemnifying party and of the indemnified party shall be determined by reference to, among other things, whether the untrue or allegedly untrue statement of a material fact, or the omission or alleged omission of a material fact, relates to information supplied by the indemnifying party or by the indemnified party and the parties' relative intent, knowledge, access to information, and opportunity to correct or prevent such statement or omission; *provided*, *however*, that, in any such case (x) Purchaser will not be required to contribute any amount in excess of the public offering price of all such Registrable Securities offered and sold by Purchaser pursuant to such registration statement, and (y) no Person guilty of fraudulent misrepresentation (within the meaning of Section 11(f) of the Securities Act) will be entitled to contribution from any Person who was not guilty of such fraudulent misrepresentation.

7.3 **Notifications.**

(a) Prior to each Closing, the Company will promptly advise Purchaser in writing of any notice or other communication from any third Person alleging that the consent of a third Person is required in connection with the transactions contemplated by this Agreement.

(b) Prior to each Closing, each party shall promptly notify the other of any action, suit or proceeding that is instituted or specifically threatened in writing against such party to restrain, prohibit or otherwise challenge the legality of any transaction contemplated by this Agreement.

7.4 **Standstill.** During the period commencing on the Effective Date and ending on the earliest of (i) five (5) years following the Effective Date, [***] neither the Purchaser nor any of Purchaser's representatives or affiliates will, in any manner, directly or indirectly:

(a) make, effect, initiate or cause (i) any [***] to the extent that [***] would result in [***], (ii) any [***] of any [***] or any [***] of the Company, (iii) any [***] involving [***], or involving [***] or any [***] or (iv) any [***] *provided*, *however*, that notwithstanding the provisions of this Section 7.4(a)(i), [***] as a result of a [***] shall not be required to [***] even though such action [***];

(b) [***] with respect to the [***];

(c) [***];

(d) [***] of this Section 7.4;

(e) [***] of this sentence;

(f) [***] of this sentence;

(g) [***]; or

(h) [***] in this Section 7.4.

Notwithstanding the foregoing, it is understood and agreed that [***] by this Section 7.4, and [***] by this Section 7.4; [***].

7.5 **Commercial Reasonable Efforts.** Each Party will use its commercially reasonable efforts to satisfy in a timely fashion each of the conditions to be satisfied by it under Section 5 and Section 6 of this Agreement.

7.6 **Securities Laws Disclosure; Publicity.** The Company shall, by 9:00 a.m. (New York City time) on the Trading Day immediately following the date hereof, issue a press release disclosing the material terms of the transactions contemplated hereby, and shall, within four (4) Trading Days following the date hereof, file a Current Report on Form 8-K disclosing the material terms of the transactions contemplated hereby and including this Agreement as an exhibit thereto. The Company and Purchaser shall consult with each other regarding the substance of any public disclosure by either party regarding this Agreement or the Collaboration Agreement (including the filing of either agreement as an exhibit to a periodic filing with the SEC) and regarding the issuance of any other press releases with respect to the transactions contemplated hereby, and neither the Company nor Purchaser shall issue any such press release nor otherwise make any such public statement without the prior consent of the Company, with respect to any press release of Purchaser, or without the prior consent of Purchaser, with respect to any press release of the Company, which consent shall not unreasonably be withheld or delayed, except if such disclosure is required by law, in which case the disclosing party shall promptly provide the other party with prior notice of such public statement or communication.

7.7 **Shareholder Rights Plan.** No claim will be made or enforced by the Company or, with the consent of the Company, any other Person, that Purchaser is an "Acquiring Person" under any control share acquisition, business combination, poison pill (including any distribution under a rights agreement) or similar anti-takeover plan or arrangement in effect or hereafter adopted by the Company, or that Purchaser could be deemed to trigger the provisions of any such plan or arrangement, by virtue of receiving Shares under this Agreement or under any other agreement among the Company and Purchaser.

7.8 **Indemnification of Purchaser.** Subject to the provisions of this Section 7.8, the Company will indemnify and hold Purchaser and its directors, officers, shareholders, members, partners, employees and agents (and any other Persons with a functionally equivalent role of a Person holding such titles notwithstanding a lack of such title or any other title), each Person who controls Purchaser (within the meaning of Section 15 of the Securities Act and Section 20 of the Exchange Act), and the directors, officers, shareholders, agents, members, partners or employees (and any other Persons with a functionally equivalent role of a Person holding such titles notwithstanding a lack of such title or any other title) of such controlling persons (each, a "**Purchaser Party**") harmless from any and all losses, liabilities, obligations, claims, contingencies, damages, costs and expenses, including all judgments, amounts paid in settlements, court costs and reasonable attorneys' fees and costs of investigation that any such Purchaser Party may suffer or incur due to a claim by a third party as a result of or relating to any action instituted against the Purchaser Parties in any capacity, or any of them or their respective Affiliates, by any stockholder of the Company who is not an Affiliate of such Purchaser Parties, with respect to any of the transactions contemplated by this Agreement (unless such action is based upon a breach of such Purchaser Party's representations, warranties or covenants under this Agreement or any agreements or understandings such Purchaser Parties may have with any such stockholder or any violations by such Purchaser Parties of state or federal securities laws or any conduct by such Purchaser Parties which constitutes fraud, gross negligence, willful misconduct or malfeasance). If any action shall be brought against any Purchaser Party in respect of which indemnity may be sought pursuant to this Agreement, such Purchaser Party shall promptly notify the Company in writing, and the Company shall have the right to assume the defense thereof with counsel of its own choosing reasonably acceptable to the Purchaser Party. Any Purchaser Party shall have the right to employ separate counsel in any such action and participate in the defense thereof, but the fees and expenses of such counsel shall be at the expense of such Purchaser Party except to the extent that (i) the employment thereof has been specifically authorized by the Company in writing, (ii) the Company has failed after a reasonable period of time to assume such defense and to employ counsel or (iii) in such action there is, in the reasonable opinion of counsel, a material conflict on any material issue between the position of the Company and the position of such Purchaser Party, in which case the Company shall be responsible for the reasonable fees and expenses of no more than one such separate counsel for all Purchaser Parties entitled to indemnification hereunder. The Company will not be liable to any Purchaser Party under this Agreement (y) for any settlement by a Purchaser Party effected without the Company's prior written consent, which shall not be unreasonably withheld or delayed; or (z) to the extent, but only to the extent that a loss, claim, damage or liability is attributable to any Purchaser Party's breach of any of the representations, warranties, covenants or agreements made by such Purchaser Party in this Agreement. The indemnity agreements contained herein shall be in addition to any cause of action or similar right of any Purchaser Party against the Company and any liabilities that the Company may be subject to pursuant to law. The Company will have the exclusive right to settle any claim or proceeding, provided that the Company will not settle any such claim, action or proceeding without the prior written consent of the Purchaser Party, which will not be unreasonably withheld or delayed; provided, however, that such consent shall not be required if the settlement includes a full and unconditional release satisfactory to the Purchaser Party from all liability arising or that may arise out of such claim or proceeding and does not include a statement as to or an admission of fault, culpability or a failure to act by or on behalf of any Purchaser Party. Notwithstanding the foregoing, in no event will the Company's liability under this Section 7.8 exceed an aggregate of
$3,000,000.

7.9 **Listing of Common Stock.** The Company hereby agrees to use commercially reasonable efforts to maintain the listing or quotation of the Common Stock on the NASDAQ Global Select Market.

7.10 **Form D; Blue Sky Filings.** The Company agrees to timely file a Form D with respect to the Shares as required under Regulation D and to provide a copy thereof, promptly upon request of

Purchaser. The Company shall take such action as the Company shall reasonably determine is necessary in order to obtain an exemption for, or to qualify the Shares for, sale to Purchaser at each Closing under applicable securities or "Blue Sky" laws of the states of the United States, and shall provide evidence of such actions promptly upon request of Purchaser.

7.11 **Book Entry Statement.** The Company hereby agrees to deliver to Purchaser a book entry statement from the Transfer Agent showing the Initial Closing Shares, Second Tranche Shares or Third Tranche Shares, as applicable, registered in the name of Purchaser within three (3) business days of the applicable Closing.

8. SURVIVAL OF REPRESENTATIONS

All representations, warranties, covenants and other agreements of the Company hereunder shall be deemed made on and as of each Closing as though such representations, warranties, covenants and other agreements were made on and as of such date. All representations and warranties made by a party to this Agreement herein or pursuant hereto shall survive each Closing and the delivery of the Shares for a period of 18 months thereafter. All covenants and other agreements made by a party to this Agreement herein or pursuant hereto shall survive until all obligations set forth therein shall have been performed or satisfied or they shall have terminated in accordance with their terms.

9. TERMINATION

9.1 **Termination.** This Agreement may be terminated at any time until the Initial Closing:

(a) by the mutual written consent of Purchaser and the Company;

(b) by the Company or the Purchaser upon termination of the Collaboration Agreement in accordance with its terms;

(c) by the Company if (i) any of the representations and warranties of Purchaser contained in Section 4 of this Agreement shall fail to be true and correct or (ii) there shall be a breach by Purchaser of any covenant of Purchaser in this Agreement that, in either case, (A) would result in the failure of a condition set forth in Section 6, and (B) which is not curable or, if curable, is not cured upon the occurrence of the twentieth (20th) day after written notice thereof is given the Company to Purchaser;

(d) by Purchaser if (i) any of the representations and warranties of the Company contained in Section 2 or Section 3 of this Agreement shall fail to be true and correct or (ii) there shall be a breach by the Company of any covenant of the Company in this Agreement that, in either case, (A) would result in the failure of a condition set forth in Section 5, and (B) which is not curable or, if curable, is not cured upon the occurrence of the twentieth (20th) day after written notice thereof is given by Purchaser to the Company; or

(e) by either Purchaser or the Company in the event that any court of competent jurisdiction or Governmental Authority shall have issued an order, decree or ruling or taken any other action restraining, enjoining or otherwise prohibiting the actions contemplated hereby and such order, decree, ruling or other action shall have become final and nonappealable.

9.2 **Effect of Termination.** In the event of any termination of this Agreement as provided in Section 9.1, this Agreement (other than Section 10, which shall remain in full force and effect) shall forthwith become wholly void and of no further force and effect; *provided* that nothing herein shall relieve any party from liability for willful breach of this Agreement.

10. GENERAL

10.1 Successors and Assigns. Except as otherwise provided herein, the terms and conditions of this Agreement shall inure to the benefit of and be binding upon the respective successors and permitted assigns of the parties (including any permitted transferees of any Shares). Purchaser and the Company may not assign their respective rights or obligations under this Agreement, in whole or in part, except with the consent of the other party; *provided*, *however*, the rights and obligations of Purchaser may be assigned, without the prior written consent of the Company, to one or more of Purchaser's affiliates. Any attempted assignment made in contravention of this Agreement shall be null and void and of no force or effect.

10.2 Entire Agreement. This Agreement and the Collaboration Agreement and the documents, schedules and exhibits referred to herein or therein constitute the entire agreement between the parties and supersede all prior communications, representations, understandings and agreements of the parties with respect to the subject matter hereof and thereof. No party shall be liable or bound to any other party in any manner by any warranties, representations or covenants except as specifically set forth herein or therein. All schedules and exhibits hereto are hereby incorporated herein by reference. Nothing in this Agreement, express or implied, is intended to confer upon any third party any rights, remedies, obligations or liabilities under or by reason of this Agreement, except as expressly provided in this Agreement.

10.3 General Interpretation. The terms of this Agreement have been negotiated by the parties hereto and the language used in this Agreement shall be deemed to be the language chosen by the parties hereto to express their mutual intent. This Agreement shall be construed without regard to any presumption or rule requiring construction against the party causing such instrument or any portion thereof to be drafted, or in favor of the party receiving a particular benefit under this Agreement. No rule of strict construction will be applied against any Person.

10.4 Injunctive Relief. Purchaser and the Company acknowledge and agree that, in view of the uniqueness of the Shares, damages at law would be insufficient for any breach by Purchaser or the Company of any of their respective covenants in this Agreement. Accordingly, each party agrees that in the event of any breach or threatened breach by the other party of any provisions of this Agreement, the non-breaching party be entitled to seek equitable relief in the form of an order to specifically perform or an injunction to prevent irreparable injury.

10.5 Governing Law. This Agreement shall be governed by and construed in accordance with the laws of the State of New York, without regard to the principles of conflicts of law thereof.

10.6 Jurisdiction. The parties hereby irrevocably and unconditionally submit to the jurisdiction of the United States District Court for the Southern District of New York for the purpose of any suit, action or other proceeding arising out of or based upon this Agreement.

10.7 Counterparts. This Agreement may be executed in any number of counterparts and by the parties hereto in separate counterparts, each of which when so executed shall be deemed to be an original and all of which taken together shall constitute one and the same agreement, and may be delivered to the other parties hereto by facsimile.

10.8 Section Headings and References. The section headings contained herein are for the convenience of the parties and in no way alter, modify, amend, limit or restrict the contractual obligations of the parties. When a reference is made in this Agreement to a Section or Exhibit, such reference is to a Section or Exhibit of or to this Agreement unless otherwise indicated. The words "hereof," "herein,"

"hereto" and "hereunder" and words of similar import, when used in this Agreement, shall refer to this Agreement as a whole and not to any particular provision of this Agreement. The terms defined in the singular has a comparable meaning when used in the plural, and vice versa. References to a Person are also to its successors and permitted assigns. References to an agreement are to such agreement as amended, restated, modified or otherwise supplemented, from time to time. The term "dollars" and "$" means United States dollars. The word "including" means "including without limitation" and the words "include" and "includes" have corresponding meanings.

10.9 **Severability.** If any term of provision of this Agreement is determined to be illegal, unenforceable or invalid in whole or in part for any reason, such illegal, unenforceable or invalid provisions or party thereof shall be stricken from this Agreement, and such provision shall not affect the legality, enforceability or validity of the remainder of this Agreement. If any provision or part thereof of this Agreement is stricken in accordance with the provisions of this Section 10.9, then such stricken provision shall be replaced, to extent possible, with a legal, enforceable and valid provision that is as similar in tenor to the stricken provision as is legally possible.

10.10 **Notices.** All notices required or permitted hereunder shall be in writing and shall be deemed effectively given: (a) upon personal delivery to the party to be notified, (b) when received by facsimile or email (provided that the party providing such notice promptly confirms receipt of such transmission with the other party), (c) when received after having been sent by registered or certified mail, return receipt requested and postage prepaid or (d) when received after deposit with a nationally recognized overnight courier, specifying next day delivery, with written verification of receipt. All communications shall be sent to the Company and to Purchaser at the address as set forth below or at such other address as Purchaser or the Company may designate by 10 days advance written notice to the Company (in the case of Purchaser) or Purchaser (in the case of the Company).

if to the Company:

Ultragenyx Pharmaceutical Inc. 60 Leveroni Ct.
Novato, CA 94949
Attn: Chief Financial Officer Facsimile:
Email:
with a copy (which shall not constitute notice) to: Cooley LLP
Attn: Glen Y Sato 3175
Hanover Street Palo Alto, CA
94304
Facsimile: (650) 849-7400 Email:
gsato@cooley.com

if to Purchaser:

Takeda Pharmaceutical Company Limited 1-1
Doshomachi 4-chome,
Chuo-ku, Osaka 540-8645
Attention: Head of Global Business Development Facsimile: (+81) 3-3278-2323

with copies (which shall not constitute notice) to:

Takeda Pharmaceuticals U.S.A., Inc. One Takeda
Parkway
Deer Field, IL 60015
Attention: General Counsel, Legal Department Facsimile: 224-554-7831

and

Morgan, Lewis & Bockius LLP
Attn: Randall B. Sunberg
Emilio Ragosa 502 Carnegie
Center
Princeton, NJ 08540
Facsimile: (609) 919-6701
Email: randall.sunberg@morganlewis.com
emilio.ragosa@morganlewis.com

10.11 **Amendments and Waivers.** Except as otherwise expressly set forth in this Agreement, any term of this Agreement may be amended and the observance of any term of this Agreement may be waived (either generally or in a particular instance and either retroactively or prospectively), only with the written consent of each party hereto (with respect to an amendment) and the written consent of each party from whom a waiver is sought (with respect to a waiver). No waiver of any provision or consent to any action shall constitute a waiver of any other provision or consent to any other action, whether or not similar. No waiver or consent shall constitute a continuing waiver or consent or commit a party to provide a waiver in the future except to the extent specifically set forth in writing.

10.12 **Expenses.** Except with respect to the registration of the Shares pursuant to Section 7.2, each party hereto will pay its own expenses in connection with the transactions contemplated hereby.

10.13 **Persons Entitled to Benefits of Agreement.** This Agreement is intended for the benefit of the parties hereto and their respective permitted successors and assigns and is not for the benefit of, nor may any provision hereof be enforced by, any other person.

10.14 **Further Assurances.** The Company and Purchaser shall use their commercially reasonable efforts, in the most expeditious manner practicable, to satisfy or cause to be satisfied the intent and purposes of this Agreement by executing and delivering such instruments, documents and other writings as may be reasonably necessary or desirable.

IN WITNESS WHEREOF, the undersigned parties have duly executed this Common Stock Purchase Agreement effective as of the date first above written.

COMPANY:

ULTRAGENYX PHARMACEUTICAL INC.

By: /s/ Emil Kakkis
Name: Emil Kakkis
Title: CEO
Date: June 6, 2016

PURCHASER:

TAKEDA PHARMACEUTICAL COMPANY LIMITED

By: /s/ Misako Hamamura
Name: Misako Hamamura
Title: Head of JP Strategy & BD
Date: June 6, 2016

Exhibit A

Collaboration and License Agreement

See attached.

LICENSE AND COLLABORATION AGREEMENT

BY AND BETWEEN

TAKEDA PHARMACEUTICAL COMPANY LIMITED AND
ULTRAGENYX PHARMACEUTICAL INC. JUNE 6, 2016

LICENSE AND COLLABORATIONAGREEMENT

This License and Collaboration Agreement (this "Agreement") is made as of the 6th day of June, 2016 (the "Execution Date") by and between **Takeda Pharmaceutical Company Limited**, a company incorporated under the laws of Japan having its principal place of business at 1-1, Doshomachi 4-chome, Chuo-ku, Osaka 540-8645, Japan ("Takeda"), and **Ultragenyx Pharmaceutical Inc.**, a company incorporated under the laws of California, having its principal place of business at 60 Leveroni Court, Novato, CA 94949, United States ("Ultragenyx"). Ultragenyx and Takeda are sometimes referred to herein individually as a "Party" and collectively as the "Parties."

RECITALS

WHEREAS, Takeda has developed certain compounds and products potentially applicable to rare genetic disease indications;

WHEREAS, Ultragenyx is a pharmaceutical company with significant experience with the development of products for rare genetic disease indications; and

WHEREAS, Ultragenyx and Takeda desire to establish a collaboration for the further development and commercialization of certain products potentially applicable to rare genetic disease and other indications.

NOW, THEREFORE, in consideration of the foregoing and the mutual agreements set forth below, and other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties agree as follows:

ARTICLE 1 – DEFINITIONS

1.1 "[***] Development Plans" has the meaning set forth in Section 4.3(b).

1.2 "[***] License Negotiation Period" has the meaning set forth in Section 5.1(a).

1.3 "[***] Option" has the meaning set forth in Section 5.1(a).

1.4 "[***] Option Term" has the meaning set forth in Section 5.1(a).

1.5 "[***] Patent Prosecution" has the meaning set forth in Section 12.3(a).

1.6 "[***] Compound" means [***].

1.7 "[***] Product" means any pharmaceutical product that contains a [***] Compound, including all forms, presentations, strengths, doses and formulations (including any method of delivery).

1.8 "[***] Research Plan" has the meaning set forth in Section 6.3(a).

1.9 "Accounting Standards" mean GAAP in the case of Ultragenyx and IFRS in the case of Takeda.

1.10 "Affiliate" means, with respect to a particular Party, a person, corporation, partnership, or other entity that controls, is controlled by or is under common control with such Party. For the purposes of this definition, the word "control" (including, with correlative meaning, the terms "controlled by" or "under the common control with") means the actual power, either directly or indirectly through one or more intermediaries, to direct or cause the direction of the management and policies of such entity, whether by the ownership of fifty percent (50%) or more of the voting stock of such entity, or by contract or otherwise.

1.11 "Agreement" has the meaning set forth in the preamble.

1.12 "Alliance Manager" means the person appointed by each Party from within their respective organization to coordinate and facilitate the communication, interaction and cooperation of the Parties pursuant to this Agreement.

1.13 "Applicable Laws" means all applicable statutes, ordinances, regulations, rules, or orders of any kind whatsoever of any Governmental Authority, including the U.S. Food, Drug and Cosmetic Act, (21 U.S.C. §301 et seq.) (the "FFDCA"), Prescription Drug Marketing Act, the Generic Drug Enforcement Act of 1992 (21 U.S.C. §335a et seq.), U.S. Patent Act (35 U.S.C. §1 et seq.), Federal Civil False Claims Act (31 U.S.C. §3729 et seq.), and the Anti-Kickback Statute (42 U.S.C. §1320a-7b et seq.), all as amended from time to time, together with any rules, regulations, and compliance guidance promulgated thereunder.

1.14 "Bankruptcy Laws" has the meaning set forth in Section 15.6(b).

1.15 "Bayh-Doyle Act" means the Patent and Trademark Law Amendments Act of 1980, as amended, codified at 35 U.S.C. §§ 200-212, as well as any regulations promulgated pursuant thereto, including 37 C.F.R. Part 401, and any successor statutes or regulations.

1.16 "[***] License Agreement" means the License Agreement by and between Ultragenyx and [***].

1.17 "Breaching Party" has the meaning set forth in Section 15.2(a).

1.18 "Bulk Drug Product" means a Product that has been Manufactured into a final pharmaceutical product, including drug substance (e.g., tablets or granules) for administration to humans in accordance with Applicable Laws, but has not been Packaged for use in Clinical Trials or for Commercialization.

1.19 "Business Day" means a day other than Saturday, Sunday or any other day on which commercial banks located in the State of New York, U.S., or Japan, are authorized or obligated by Applicable Laws to close.

1.20 "Calendar Quarter" means the respective periods of three (3) consecutive calendar months ending on March 31, June 30, September 30 and December 31; provided, however, that
(a) the first Calendar Quarter of the Term shall extend from the Effective Date to the end of the first complete Calendar Quarter thereafter; and (b) the last Calendar Quarter of the Term shall end upon the expiration or termination of this Agreement.

1.21 "Calendar Year" means the twelve-month period ending on December 31; provided however, that (a) the first Calendar Year of the Term, shall begin on the Effective Date and end on December 31, 2016; and (b) the last Calendar Year of the Term shall end on the date of expiration or termination of this Agreement.

1.22 "Candidate Product" has the meaning set forth in Section 6.2(a).

1.23 "Change of Control" of Ultragenyx means if: (a) any Third Party acquires directly or indirectly the beneficial ownership of any voting security of Ultragenyx, or if the percentage ownership of such person or entity in the voting securities of Ultragenyx is increased through stock redemption, cancellation or other recapitalization, and immediately after such acquisition or increase such Third Party is, directly or indirectly, the beneficial owner of voting securities representing [***] of the total voting power of all of the then- outstanding voting securities of Ultragenyx; (b) [***], which would result in stockholders or equity holders of Ultragenyx, or an Affiliate of Ultragenyx, immediately prior to such transaction [***] of the surviving entity (or its parent entity) immediately following such transaction; (c) the stockholders or equity holders of Ultragenyx approve [***], other than pursuant to the transaction as described above or to an Affiliate; or (d) the sale or other transfer to a Third Party of [***].

1.24 "Claim" has the meaning set forth in Section 17.1.

1.25 "Clinical Trial" means any human clinical study or trial of a pharmaceutical product in the Licensed Field in the Territory, including Phase I Trials, Phase II Trials, Phase III Trials and Phase IV Trials.

1.26 "Collaboration Activities" has the meaning set forth in Section 2.2(a).

1.27 "Collaboration Term" means (a) with respect to [***] from the Effective Date and (b) other than with respect to [***], unless, in case of each of the foregoing clauses (a) or (b), (i) extended by mutual agreement of the Parties, or (ii) terminated earlier in accordance with the terms of this

Agreement; provided that if at the expiration of the foregoing period, an Option Negotiation Period is then ongoing, the Collaboration Term with respect to such Option Product will automatically extend until the earlier of (A) expiration of such Option Negotiation Period or (B) execution of the applicable Option Product License Agreement.

1.28 "Combination Product" means a Product that is comprised of or contains a Compound as an active ingredient together with one (1) or more other active ingredients and is sold by a Party, or any of its Affiliates or sublicensees, either as a fixed dose or as separate doses as one (1) product.

1.29 "Commercialization" means all activities undertaken in support of the promotion, marketing, sale and distribution (including importing, exporting, transporting, customs clearance, warehousing, invoicing, handling and delivering the applicable Product to customers) of the applicable Product, including Manufacturing Product for commercial sale, sales force efforts, detailing, advertising, marketing, the creation and approval of Promotional Materials, sales and distribution, pricing, customer and government contracting, and medical affairs, including medical education, medical information, clinical science liaison activities, health economics and outcomes research, publications and investigator initiated research studies. "Commercialize" means to engage in Commercialization activities.

1.30 "Commercialization Plan" means, as applicable, (a) a plan prepared by Ultragenyx pursuant to Section 5.3 containing an overview of the general strategy and a high-level budget for the promoting and marketing of the Licensed Products in the Ultragenyx Field in the Territory or (b) a plan prepared by Takeda pursuant to Section 5.3 containing an overview of the general strategy for the promoting and marketing of the Licensed [***] Product in the Takeda Field in the Territory.

1.31 "Commercially Reasonable Efforts" means with respect to the efforts to be expended, or considerations to be undertaken, by a Party or its Affiliates with respect to any objective, activity or decision to be undertaken under this Agreement with respect to the Compounds or Products, the commercially reasonable efforts, expertise, and resources commonly used by such Party for a product owned by it or to which it has exclusive rights in the applicable territory, which, as compared with a Product, is of similar market potential, at a similar stage in its development or product life, and involves similar risks, all as measured based upon the facts and circumstances at the time such efforts are due, taking into account issues of: efficacy and safety, the competitiveness of alternative products sold by Third Parties, the product profile (including Labeling), the proprietary protection and regulatory exclusivity, the expected and actual profitability and return on investment, and all other similar relevant factors.

1.32 "Committee" has the meaning set forth in Section 2.3(a).

1.33 "Common Stock Purchase Agreement" means the common stock purchase agreement entered into on even date hereof by and between Ultragenyx and Takeda (or one of its Affiliates) providing for Takeda's (or one of its Affiliate's) purchase of common stock of Ultragenyx.

1.34 "Competing Product" means [***].

1.35 "Compound" means the Licensed [***] Compound, a Licensed Analog Compound, [***] Compound, Candidate Product or Ultragenyx Pipeline Compound, as applicable.

1.36 "Confidential Information" means all non-public or proprietary Information disclosed by a Party to the other Party under this Agreement, which may include ideas, inventions, discoveries, concepts, compounds, compositions, formulations, formulas, practices, procedures, processes, methods, knowledge, know-how, trade secrets, technology, inventories, machines, techniques, development and commercialization plans and related information, designs, drawings, computer programs, skill, experience, documents, apparatus, results, clinical and regulatory strategies, regulatory documentation, information and submissions pertaining to, or made in association with, filings with any Regulatory Authority, data, including pharmacological, toxicological and clinical data, analytical and quality control data, manufacturing data and descriptions, Patent and legal data, market data, financial data or descriptions, devices, assays, chemical formulations, specifications, material, product samples and other samples, physical, chemical and biological materials and compounds, and the like, without regard as to whether any of the foregoing is marked "confidential" or "proprietary," or disclosed in oral, written, graphic, or electronic form. Confidential Information shall include: (a) the terms and conditions of this Agreement; and (b) Confidential Information disclosed by either Party pursuant to the Confidentiality Agreement.

1.37 "Confidentiality Agreement" means the Mutual Confidential Disclosure Agreement dated March 13, 2015 by and between Takeda Pharmaceuticals International, Inc. and Ultragenyx Pharmaceutical Inc.

1.38 "Control" means, with respect to any Information, Patent, trademark or other intellectual property right, ownership or possession by a Party, including its Affiliates, of the ability (without taking into account any rights granted by one Party to the other Party under the terms of this Agreement) to grant access, a license or a sublicense to such Information, Patent, trademark or other intellectual property right without violating the terms of any agreement or other arrangement with, or necessitating the consent of, any Third Party, at such time that the Party would be first required under this Agreement to grant the other Party such access, license or sublicense.

1.39 "Cover", "Covering" or "Covered" means, with respect to a product, technology, process or method, that, in the absence of ownership of or a license granted under a Valid Claim, the practice or Exploitation of such product, technology, process or method would infringe such Valid Claim (or, in the case of a Valid Claim that has not yet issued, would infringe such Valid Claim if it were to issue).

1.40 "Cure Period" has the meaning set forth in Section 15.2(a).

1.41 "Data Package" means the Final [***] Data Package, Final Phase II Data Package or Final Phase III Data Package, as applicable.

1.42 "Development" means all non-clinical and clinical drug development activities, including toxicology, pharmacology, and other non-clinical efforts, statistical analysis, the performance of Clinical Trials, including the Manufacturing of the applicable Product for use in the Clinical Trials, or other activities necessary to obtain or maintain, Regulatory Approval of the applicable Products. "Development" shall exclude Commercialization activities. When used as a verb, "Develop" means to engage in Development activities.

1.43 "Disclosing Party" has the meaning set forth in Section 14.1.

1.44 "Dispute" has the meaning set forth in Section 16.1.

1.45 "Effective Date" means the date this Agreement becomes effective, as determined in accordance with Section 18.1.

1.46 "EMA" means the European Medicines Agency or any successor agency or authority having substantially the same function.

1.47 "EU" means all of the European Union member states as of the applicable time during the Term.

1.48 "Execution Date" has the meaning set forth in the preamble.

1.49 "Exercised Countries" has the meaning set forth in Section 8.2(c).

1.50 "Exercised Product License Agreement" has the meaning set forth in Section 8.2(d).

1.51 "Exercised Products" has the meaning set forth in Section 8.2(c).

1.52 "Expert" means a disinterested, conflict-of-interest-free individual who is neutral and independent of both Parties and all of their respective Affiliates and sublicensees and who, with respect to a dispute concerning a financial, commercial, scientific or regulatory matter, possesses appropriate expertise to resolve such dispute. Neither the Expert (nor any of the Expert's current or former employers) shall be or have been at any time, to the Knowledge of the Parties, an employee, officer, director or, during the previous five (5) years, a consultant or contractor of either Party or any of its Affiliates.

1.53 "Exploit" or "Exploitation" means to research, import, Manufacture, have Manufactured, export distribute, use, have used, sell, have sold, or offer for sale, including to Develop, Commercialize, register, modify, enhance, improve or otherwise dispose of.

1.54 "FDA" means the U.S. Food and Drug Administration, or any successor agency thereto.

1.55 "Final [***] Data Package" means all information the Parties agree that Ultragenyx shall provide to or give access to Takeda at the conclusion of the activities contemplated under the Initial [***] Development Plan for a given Licensed [***] Product as it relates to the Takeda Field, but which will include at a minimum (a) validated and reproducible tables, listings and graphs,
(b) all adverse event listings, safety narratives, CMC data and information, and applicable

Regulatory Documentation, (c) preclinical study results and final, if possible, or preliminary toxicology and pharmacology reports, and (d) a preliminary Phase I report and all Phase I clinical data.

1.56 "Final Phase II Data Package" means on a Product-by-Product basis, all Information the Parties agree that Ultragenyx shall provide to or give access to Takeda at the conclusion of a Phase II Clinical Trial and after database lock, but which will include at a minimum (a) validated and reproducible tables, listings and graphs, (b) all adverse event listings, safety narratives, CMC data and information, and applicable Regulatory Documentation, (c) final, if possible, or preliminary toxicology and pharmacology reports, (d) the Phase I final report and all Phase I clinical data, and (e) a preliminary Phase II report and all Phase II clinical data.

1.57 "Final Phase III Data Package" means, on a Product-by-Product basis, all Information the Parties agree that Ultragenyx shall provide to or give access to Takeda at the conclusion of a Phase III Clinical Trial and after database lock, but which will include at a minimum (a) validated and reproducible tables, listings and graphs, (b) all adverse event listings, material safety narratives, CMC data and information, and applicable Regulatory Documentation, (c) final, if possible, or preliminary toxicology and pharmacology reports, (d) the Phase I final report and all Phase I clinical data to the extent not previously provided to Takeda, (e) the Phase II final report and all Phase II clinical data to the extent not previously provided to Takeda, and (f) the preliminary Phase III report and all Phase III clinical data.

1.58 "Finished Product" means Bulk Drug Product that has been Packaged into a form suitable for use in Clinical Trials or for Commercial purposes (i.e., bottles or blisters), including samples, in accordance with Applicable Laws.

1.59 "First Commercial Sale" means, on a country-by-country basis, the first sale of a Product under this Agreement by a Party, its Affiliates or its sublicensees to an end user or prescriber for use, consumption or resale of the Product in a country in the applicable territory in the applicable field where Regulatory Approval of the Product has been obtained and where the sale results in a recordable Net Sale. Sale of a Product under this Agreement by a Party to an Affiliate or a sublicensee of such Party shall not constitute a First Commercial Sale unless such Affiliate or such sublicensee is the end user of such Product. Also, sale of a Product under this Agreement by a Party, its Affiliates or its sublicensees in a jurisdiction where Regulatory Approval for that Product has not yet been attained shall not constitute a First Commercial Sale under this Agreement.

1.60 Force Majeure" means any event beyond the reasonable control of the affected Party including: embargoes; war or acts of war, including terrorism; insurrections, riots, or civil unrest; strikes, lockouts or other labor disturbances; epidemics, fire, floods, earthquakes or other acts of nature; or acts, omissions or delays in acting by any governmental authority (including the refusal of the competent government agencies to issue required Regulatory Approvals due to reasons other than the affected Party's negligence or willful misconduct or any other cause within the reasonable control of the affected Party), and failure of plant or machinery (provided that such failure could not have been prevented by the exercise of skill, diligence, and prudence

that would be reasonably and ordinarily expected from a skilled and experienced person engaged in the same type of undertaking under the same or similar circumstances).

1.61 "FTE" means eighteen hundred (1800) hours of work per full Calendar Year (or equivalent pro-rata portion thereof for a period less than twelve (12) months) devoted to or in support of the Development of the applicable Products in accordance with the Research Plans or the Manufacturing of a Product or the provision of Research Support (but excluding, for clarity, time spent travelling to and attending meetings under this Agreement and scientific and medical conferences), that is carried out by one or more qualified scientific or technical employees or contract personnel of Takeda or its Affiliates, as such hours are measured in accordance with Takeda's normal time allocation practices. For the avoidance of doubt, FTE only applies to employees of a Party, and does not apply to contractors of Takeda.

1.62 "FTE Cost" means, for any period, the FTE Rate multiplied by the number of FTEs in such period.

1.63 "FTE Rate" means a rate of [***] per FTE per Calendar Year (pro-rated for the period beginning on the Effective Date and ending at the end of the first Calendar Year) for personnel engaged in Development activities. Such rate shall be adjusted annually, with each annual adjustment effective as of January 1 of each calendar year (with the first such annual adjustment to be made as of January 1, 2018) to correspond with the total percentage change in the Consumer Price Index for All Urban Consumers (CPI-U) for the U.S. City Average, 1982-84 = 100, calculated by the U.S. Bureau of Labor Statistics over the twelve (12)-month period preceding each such January 1.

1.64 "GAAP" means generally accepted accounting principles current in the U.S.

1.65 "Generic Competition Percentage" means, with respect to any Product in a given country in the Territory or Takeda Territory (as applicable), all units of the Generic Product(s) for such Product, sold in the aggregate in such country divided by the sum of: (a) all units of the Product sold in such country, and (b) all units of the Generic Product(s) sold in the aggregate in such country, where, in each case, the number of units of a Product and each Generic Product sold shall be based on the average of the monthly IMS data (or IMS-equivalent data if IMS data are not available).

1.66 "Generic Product" means, on a Product-by-Product and country-by-country basis, any pharmaceutical product sold by a Third Party, other than as a sublicensee to this Agreement that:
(a) contains the same active ingredients as the applicable Product, in the same dosage form (e.g., oral) as the applicable Product; or (b) is A/B Rated with respect to such Product or otherwise approved by the Regulatory Authority in such country as a substitutable generic for such Product; or (c) is approved in the applicable field by a Regulatory Authority pursuant to an NDA filed by a Third Party under Section 505(b)(2) or 505(j)(2) of the FFDCA (or an equivalent Regulatory Approval Application filed outside the U.S.), contains the active ingredients in the Product, and relies on the finding of safety and/or effectiveness in the Regulatory Approval of the Product. For the purposes of this definition, "A/B Rated" means, inside the U.S., "therapeutically equivalent" as determined by the FDA, applying the definition of

"therapeutically equivalent" set forth in the preface to the then-current edition of the FDA publication "Approved Drug Products With Therapeutic Equivalence Evaluations and, outside the U.S., such equivalent determination by the applicable Regulatory Authorities as is necessary to permit pharmacists or other individuals authorized to dispense pharmaceuticals under Applicable Law to substitute one product for another product in the absence of specific instruction from a physician or other authorized prescriber under Applicable Law."

1.67 "Good Clinical Practices", "GCP" or "cGCP" means the then-current standards, practices and procedures promulgated or endorsed by the FDA as set forth in the guidelines adopted by the International Conference on Harmonization ("ICH"), titled "Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance," (or any successor document) including related regulatory requirements imposed by the FDA and comparable regulatory standards, practices and procedures promulgated by the EMA, PMDA or other Regulatory Authority applicable to the Territory, as they may be updated from time to time.

1.68 "Good Laboratory Practices", "GLP", or "cGLP" means the then-current standards, practices and procedures promulgated or endorsed by the FDA as set forth in 21 C.F.R. Part 58 (or any successor statute or regulation), including related regulatory requirements imposed by the FDA and comparable regulatory standards, practices and procedures promulgated by the EMA, PMDA or other Regulatory Authority applicable to the Territory, as they may be updated from time to time, including applicable guidelines promulgated under the ICH.

1.69 "Good Manufacturing Practices", "GMP", or "cGMP" means the then-current good manufacturing practices required by the FDA, as set forth in the FFDCA, as amended, and the regulations promulgated thereunder, for the manufacture and testing of pharmaceutical materials, and comparable Applicable Law related to the manufacture and testing of pharmaceutical materials in jurisdictions outside the U.S., including the quality guideline promulgated by the ICH designated ICH Q7A, titled "Q7A Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients" and the regulations promulgated thereunder, in each case as they may be updated from time to time.

1.70 "Governmental Authority" means any multi-national, federal, state, local, municipal or other government authority of any nature (including any governmental division, subdivision, department, agency, bureau, branch, office, commission, council, court or other tribunal).

1.71 "Hatch-Waxman Act" means the Drug Price Competition and Patent Term Restoration Act, 21 U.S.C. 355, as amended

1.72 "House Mark" means the trademark that a Party uses to identify its commercial operations.

1.73 "HSR Act" means the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended, and the rules promulgated thereunder.

1.74 "HSR Conditions" means the following conditions, collectively: (a) the waiting period under the HSR Act shall have expired or earlier been terminated; (b) no injunction (whether

temporary, preliminary or permanent) prohibiting consummation of the transaction contemplated by this Agreement or any material portion hereof shall be in effect; (c) no judicial or administrative proceeding opposing consummation of all or any part of this Agreement shall be pending; and (d) no requirements or conditions shall have been imposed by the United States Department of Justice or Federal Trade Commission (as applicable) in connection with the filings by the Parties under the HSR Act, other than requirements or conditions that are satisfactory to the Party on whom such requirements or conditions are imposed.

1.75 "HSR Filing" means filings with the United States Federal Trade Commission and the Antitrust Division of the United States Department of Justice of a Notification and Report Form for Certain Mergers and Acquisitions (as that term is defined in the HSR Act) with respect to the subject matter of this Agreement, together with all required documentary attachments thereto.

1.76 "IFRS" means the International Financial Reporting Standards as promulgated by the International Standards Accounting Board and as they may be updated for time to time.

1.77 "IND" means an Investigational New Drug application as defined in the FFDCA, as amended, and applicable regulations promulgated hereunder by the FDA, or a clinical trial authorization application for a product filed with a Regulatory Authority in any other regulatory jurisdiction outside the U.S., the filing of which is necessary to commence or conduct clinical testing of a pharmaceutical product in humans in such jurisdiction.

1.78 "IND Date" means the date on which ownership of Product INDs is transferred or a right of reference is granted pursuant to Section 9.2(a)(i), in the case of transfers or grants to Ultragenyx, or pursuant to Section 9.2(b)(i), in the case of transfers to Takeda..

1.79 "Indemnifying Party" has the meaning set forth in Section 17.3(a).

1.80 "Indemnitee" has the meaning set forth in Section 17.3(a).

1.81 "Information" means information, Inventions, discoveries, compounds, compositions, formulations, formulas, practices, procedures, processes, methods, knowledge, trade secrets, technology, techniques, designs, drawings, correspondence, computer programs, documents, apparatus, results, strategies, regulatory documentation, information and submissions pertaining to, or made in association with, filings with any Regulatory Authority or patent office, data, including pharmacological, toxicological, non-clinical and clinical data, analytical and quality control data, manufacturing data and descriptions, market data, financial data or descriptions, devices, assays, chemical formulations, specifications, material, product samples and other samples, physical, chemical and biological materials and compounds, and the like, in written, electronic, oral or other tangible or intangible form, now known or hereafter developed, whether or not patentable.

1.82 "Initial [***] Development Plan" means the plan (including timeline and budget) covering preliminary Development activities to be completed by Ultragenyx and Takeda (to the extent expressly provided in such plan) for a Licensed [***] Product in the Licensed Field attached

hereto as Exhibit 1.82, as such plan may be amended from time to time pursuant to Section 2.1(a)(v).

1.83 "Inventions" means any and all inventions, discoveries and developments, whether or not patentable, made, conceived or reduced to practice in the course of performance of this Agreement, whether made, conceived or reduced to practice solely by, or on behalf of, Takeda, Ultragenyx, the Parties jointly, or any Affiliate of the same.

1.84 "Joint Know-How" means all Information included in the Joint Inventions.

1.85 "Joint Intellectual Property" means, collectively, Joint Know-How and Joint Patents.

1.86 "Joint Invention" has the meaning set forth in Section 12.1(b).

1.87 "Joint Patents" has the meaning set forth in Section 12.3(c).

1.88 "Joint Research Committee" or "JRC" has the meaning set forth in Section 2.2(a).

1.89 "Joint Steering Committee" or "JSC" has the meaning set forth in Section 2.1(a).

1.90 "Knowledge" means, as applied to a Party, that such Party shall be deemed to have knowledge of a particular fact or other matter to the extent that a person within the Knowledge Group knew of such fact or other matter.

1.91 "Knowledge Group" means, with respect to each Party, the individuals holding the positions listed on Exhibit 1.91; provided that if one or more of the individuals listed on Exhibit
1.191 no longer holds the same position or title set forth opposite his/her name, (a) such person shall continue to be considered part of the Knowledge Group, and (b) his/her replacement shall also be considered part of the Knowledge Group.

1.92 "Labeling" means the healthcare professional information or patient information used in the Territory that is part of the Product Regulatory Approval including the package insert, medication guides, company core safety information (CCSI) and company core data sheet (CCDS).

1.93 "Lead Regulatory Party" has the meaning set forth in Section 9.1.

1.94 "Licensed [***] Compound" means [***] as further described on, and with the chemical structure set forth in, Exhibit 1.94.

1.95 "Licensed [***] Know-How" means Information related to the (a) Licensed [***] Compound, Controlled by Takeda as of the Execution Date or during the Term, and/or (b) Licensed Analog Compound specified in the Agreement Controlled by Takeda as of the Execution Date, in each case including data, reports, and materials related to preclinical studies, regulatory filings/correspondence, and chemistry, manufacturing and controls and necessary or

reasonably useful for the Exploitation of a Licensed [***] Compound or a Licensed Analog Compound.

1.96 "Licensed [***] Patent" means the Patent that is Controlled by Takeda as of the Execution Date identified as the Licensed [***] Patent on Exhibit 1.168, and all Patents Controlled by Takeda during the Term that claim priority to such Patent.

1.97 "Licensed [***] Product" means any pharmaceutical product that contains the Licensed [***] Compound, including all forms, presentations, strengths, doses and formulations (including any method of delivery).

1.98 "Licensed [***] Technology" means the Licensed [***] Patent and Licensed [***] Know- How.

1.99 "Licensed Analog Compounds" means (a) the compounds with the chemical structures listed on Exhibit 1.99 and (b) any structures defined by [***] where approved by the JSC pursuant to Section 2.1(a)(iii)) [***], that are disclosed in the Licensed [***] Patent and that are developed pursuant to, and as specified in, a mutually agreed research plan conducted by Ultragenyx involving modifications to such structures. Exhibit 1.99 shall be updated from time to time to include those chemical structures described in the foregoing subclause (b).

1.100 "Licensed Analog Product" means any pharmaceutical product that contains a Licensed Analog Compound, including all forms, presentations, strengths, doses and formulations (including any method of delivery).

1.101 "Licensed Field" means [***].

1.102 "Licensed Option Product" means any Option Product for which the Parties have executed an Option Product License Agreement.

1.103 "Licensed Product" means the Licensed [***] Products and Licensed Analog Products, as applicable.

1.104 "Licensed Product Improvement" means any Invention related to the Licensed [***] Compound, Licensed Analog Compounds, or Licensed Products made (a) solely by, or on behalf of, Ultragenyx or its Affiliates or sublicensees under this Agreement or (b) solely by Takeda or its Affiliates under this Agreement. For clarity, (i) employees of Ultragenyx or its Affiliates or sublicensees, or their respective agents or independent contractors receiving consideration from Ultragenyx or its Affiliates or sublicensees in the course of conducting activities under this Agreement, shall be considered "solely by, or on behalf of" pursuant to this Section 1.104, and
(ii) neither Takeda nor any of its Affiliates shall, under any circumstances under this Agreement, be considered an agent or independent contractor of Ultragenyx or any of its Affiliates or sublicensees for purposes of this Section 1.104.

1.105 "Licensed Product Improvement Patents" means Patents that Cover Licensed Product Improvements that do not claim priority (in accordance with Section 1.129) to the Licensed [***] Patent.

1.106 "Licensed Product Royalty Term" means, on a country-by-country and Licensed Product- by-Licensed Product basis, the period commencing on the First Commercial Sale of such Licensed Product in such country in the Territory and ending upon the later of (a) [***] years after First Commercial Sale of such Licensed Product in such country, (b) the expiration in such country of the last Valid Claim from the Licensed [***] Patent that Covers the composition, or method of making or using, such Licensed Product, or (c) the expiration of the applicable Regulatory Exclusivity of a Licensed Product.

1.107 "Listed Compounds" has the meaning set forth in Section 6.1.

1.108 "Loss" has the meaning set forth in Section 17.1.

1.109 "Marketing Authorization Application" or "MAA" means an application for Regulatory Approval (but excluding Pricing Approval) in any particular jurisdiction other than the U.S.

1.110 "Manufacture" means all activities related to the manufacturing of a Finished Product or Bulk Drug Product, including the manufacture of any ingredient used therein, for Development or Commercialization in the Territory, packaging, in-process and Product testing, validation, release of Product or any component or ingredient thereof, quality assurance activities related to manufacturing and release of Product, ongoing stability tests, Packaging of Bulk Drug Product into Finished Product and regulatory activities related to any of the foregoing.

1.111 "NDA" means a New Drug Application or supplemental New Drug Application as contemplated by Section 505(b) of the FFDCA, as amended, and the regulations promulgated thereunder, submitted to the FDA pursuant to Part 314 of Title 21 of the U.S. Code of Federal Regulations, including any amendments thereto.

1.112 "Net Sales" means, with respect to any Product and calculated in accordance with Accounting Standards consistently applied across Products, the gross revenue recognized by a Party, its Affiliates and sublicensees for sales of such Product to Third Parties, less the following deductions, to the extent such deductions are paid, incurred or otherwise taken, reasonable and customary, provided to Third Parties, and actually allowed with respect to such sales:

(a) reasonable cash, trade or quantity discounts, charge-back payments, and rebates actually granted to trade customers, managed health care organizations, pharmaceutical benefit managers, group purchasing organizations and national, state, or local government; and

(b) credits, rebates or allowances actually allowed upon prompt payment or on account of claims, damaged goods, rejections or returns of such Product, including in connection with recalls, and the actual amount of any write-offs for bad debt (not to exceed one percent (1%)) (provided that an amount subsequently recovered will be treated as Net Sales)

(c) inventory management fees and costs of freight, carrier insurance, and other transportation charges directly related to the distribution of such Product; and

(d) taxes, duties or other governmental charges (including (i) any tax such as a value added or similar tax, other than any taxes based on income, and (ii) any payments made to the Pharmaceutical and Medical Device Agency ("*Kiko*") based on Section 19 or 22 of the "Act on Pharmaceuticals and Medical Devices Agency (Act No.192 of 2002)") directly levied on or measured by the billing amount for such Product, as adjusted for rebates and refunds.

Notwithstanding the foregoing, amounts received or invoiced by a Party, its Affiliates or sublicensees for the sale of such Product among a Party, its Affiliates or sublicensees for resale shall not be included in the computation of Net Sales hereunder. In any event, any amounts received or invoiced by a Party, its Affiliates and sublicensees shall be accounted for only once. For purposes of determining Net Sales, a Product shall be deemed to be sold when the revenue generated from such sale is recognized in accordance with the Accounting Standards. Each Party shall record such Net Sales as the "principal" and not the "agent" as defined under the Accounting Standards. For clarity, a particular deduction may only be accounted for once in the calculation of Net Sales and no deductions may be made for the annual fee on prescription drug manufacturers imposed by the Patient Protection and Affordable Care Act, Pub. L. No. 111-148 (as amended). Net Sales shall exclude any samples of a Product transferred or disposed of at no cost for promotional, Development or educational purposes.

The Net Sales of any Combination Product:

(i) for which the Product(s) and other active ingredient(s) of such Combination Product are sold separately by a Party, or any of its Affiliates or sublicensees, in such country, then Net Sales for such Combination Product in such country shall be calculated by multiplying actual Net Sales of such Combination Product in such country by the fraction A/(A+B), where A is the average Net Sales price of the Product as the only active ingredient(s), as sold separately by a Party or any of its Affiliates or sublicensees in such country, and B is the average net sales (calculated in a manner analogous to the manner in which Net Sales are calculated as set forth above) price of the other active ingredient(s) in the Combination Product as sold separately by a Party or any of its Affiliates or sublicensees in such country;

(ii) for which the (A) Licensed Product of such Combination Product is/are sold separately by a Party or any of its Affiliates or sublicensees in such country and (B) the other active ingredient(s) in the Combination Product is/are not sold separately by a Party or any of its Affiliates or sublicensees in such country, then Net Sales for such Combination Product in such country shall be calculated by multiplying actual Net Sales of such Combination Product in such country by the fraction A/D, where A is the average Net Sales price of the Licensed Product as the only active ingredient(s), as sold separately by a Party or any of its Affiliates or sublicensees in such country, and D is the average Net Sales price of the Combination Product as sold separately by a Party or any of its Affiliates or sublicensees in such country; and

(iii) for which neither clause (i) nor clause (ii) above is applicable, the Parties shall determine Net Sales for such Combination Product in such country by mutual agreement

based on the relative contribution of the Licensed Product and the other active ingredient(s) in the Combination Product.

1.113 "Neutral Expert" has the meaning set forth in Section 16.3(a).

1.114 "Non-breaching Party" has the meaning set forth in Section 15.2(a).

1.115 "Notice Date" has the meaning set forth in Section 16.3(a).

1.116 "Option Negotiation Period" has the meaning set forth in Section 6.12(a).

1.117 "Option Notice" has the meaning set forth in Section 6.12(a).

1.118 "Option Product" means (a) a Candidate Product selected pursuant to Section 6.10 or (b) a [***] Product, as applicable.

1.119 "Option Product Improvements" means any Invention related to a [***] Product or another Research Product made (a) solely by, or on behalf of, Ultragenyx or its Affiliates or sublicensees under this Agreement, or (b) solely by Takeda or its Affiliates under this Agreement. For clarity,
(i) employees of Ultragenyx or its Affiliates or sublicensees, or their respective agents or independent contractors receiving consideration from Ultragenyx or its Affiliates or sublicensees in the course of conducting activities under this Agreement, shall be considered "solely by, or on behalf of" pursuant to this Section 1.119, and (ii) neither Takeda nor any of its Affiliates shall, under any circumstances under this Agreement, be considered an agent or independent contractor of Ultragenyx or any of its Affiliates or sublicensees for purposes of this Section 1.119.

1.120 "Option Product Improvement Patents" means Patents Covering Option Product Improvements.

1.121 "Option Product Key Terms" has the meaning set forth in Section 6.10(a).

1.122 "Option Product Know-How" means all Information Controlled by Takeda as of the Execution Date and during the Term that is necessary or reasonably useful for, as applicable, (a) Ultragenyx to evaluate whether to exercise the Ultragenyx Option or (b) Ultragenyx to Exploit an Option Product solely in accordance with the activities to be performed by Ultragenyx or its Affiliates or sublicensees under the Option Product Research Plan.

1.123 "Option Product License Agreement" has the meaning set forth in Section 6.12(a).

1.124 "Option Product Patents" means all Patents Controlled by Takeda as of the Execution Date and during the Term that are necessary or reasonably useful for the Exploitation of the Option Product(s) in the Ultragenyx Field in the Territory.

1.125 "Option Product Research Plan" has the meaning set forth in Section 6.10(a).

1.126 "Option Product Technology" means the Option Product Patents and Option Product Know-How.

1.127 "Packaging" means all activities related to the preparation of Bulk Drug Product into Finished Product, including application of the approved Labeling. "Packaged" means that Bulk Drug Product has been subject to complete Packaging.

1.128 "Party" has the meaning set forth in the preamble.

1.129 "Patents" means all patents, including any utility or design patent, and all applications thereof, including any provisional application, whether in the Territory or any other jurisdiction; any other patent or patent application claiming priority to (a) any such specified patent or patent application or (b) any patent or patent application from which such specified patent or patent application claim priority; and (c) all divisionals, continuations, continuations in-part, registrations, reissues, re-examinations, renewals, supplemental protection certificates, or extensions of (a) or (b).

1.130 "Patent Term Extension" means any term extensions, supplementary protection certificates and equivalents thereof offering Patent protection beyond the initial term with respect to any issued Patents.

1.131 "Person" means an individual, sole proprietorship, partnership, limited partnership, limited liability partnership, corporation, limited liability company, business trust, joint stock company, trust, incorporated association, joint venture or similar entity or organization, including a government or political subdivision, department or agency of a government.

1.132 "Phase I Trial" means a clinical trial of a Product with the endpoint of determining initial tolerance, safety, pharmacokinetic or pharmacodynamic information in single dose, single ascending dose, multiple dose and/or multiple ascending dose regimens.

1.133 "Phase II Trial" means a clinical trial of a Product on patients, including possibly pharmacokinetic, pharmacodynamic and dose-ranging studies, the principal purposes of which are to make a preliminary determination that such product is safe for its intended use and to obtain sufficient information about such product's efficacy or dose-response information to permit the design of further clinical trials.

1.134 "Phase III Trial" means a pivotal clinical trial of a Product on a sufficient number of patients, which trial is designed to (a) establish that a product is safe and efficacious for its intended use; (b) define warnings, precautions and adverse reactions that are associated with the product in the dosage range to be prescribed; and (c) pivotal to support submission of a Regulatory Approval Application for such product.

1.135 "Phase IV Trial" means a clinical trial of a Product, including pharmacokinetic studies, which trial (a) is not required in order to obtain Regulatory Approval of an indication; and (b) either (i) is required by the Regulatory Authority as mandatory to be conducted on or after the Regulatory Approval of an indication, or (ii) is conducted voluntarily to enhance marketing or scientific knowledge of the product (e.g., providing additional drug profile, outcomes research, safety data or marketing support information, or supporting expansion of product labeling).

1.136 "PMDA" means Japan's Pharmaceuticals and Medical Devices Agency and any successor agency(ies) or authority having substantially the same function.

1.137 "Preexisting Third Party IP" means those intellectual property rights owned or controlled by Third Parties as of the Execution Date that are necessary or reasonably useful for the Exploitation of Licensed Products and which are set forth in Exhibit 1.137.

1.138 "Pricing Approval" means governmental approval, agreement, determination or decision establishing prices that can be charged and/or reimbursed for a Product in a jurisdiction where the applicable Governmental Authority or Regulatory Authority approves or determines the pricing of pharmaceutical products.

1.139 "Product" means any Licensed [***] Product, Licensed Analog Product, Licensed Option Product or Ultragenyx Pipeline Product, as applicable.

1.140 "Product Complaint" means all data, which come to the attention of either Party, its Affiliates or its sub-licensees, concerning any dissatisfaction regarding a Product of such a nature and magnitude that it is required under Applicable Laws to be collected, maintained and reported to a Regulatory Authority, including reports of actual or suspected product tampering, contamination, mislabeling or inclusion of improper ingredients.

1.141 "Product IND" means any IND filed in the Territory related to a Product, whether in existence as of the Effective Date or filed with the FDA during the Term, including any supplements or amendments thereto. The Product INDs as of the Execution Date are set forth on Exhibit 1.141.

1.142 "Product Liabilities" means all losses, damages, fees, costs and other liabilities incurred by a Party, its Affiliate or its sublicensee and resulting from or relating to the any use of a Compound and/or a Product in a human (including in Clinical Trials and/or pursuant to Commercialization) in the Territory, other than any losses, damages, fees, costs and other liabilities that are a result of a Party's, its Affiliates' or its sublicensee's negligence, willful misconduct or breach of such Party's representations and warranties made hereunder. For the avoidance of doubt, Product Liabilities include, reasonable attorneys' and experts' fees and costs relating to any claim or potential claim against a Party, its Affiliate, or its sublicensee and all losses, damages, fees, costs. Product Liabilities shall not include liabilities associated with recalls and/or the voluntary or involuntary withdrawal of the Compound and/or a Product.

1.143 "Promotional Materials" means all written, printed, graphic, electronic, audio or video presentations of information, including journal advertisements, sales visual aids, formulary binders, reprints, direct mail, direct-to-consumer advertising, disease awareness materials, internet postings, broadcast advertisements and sales reminder aides (for example, note pads, pens and other such items, if appropriate) intended for use or used by or on behalf of a Party, its Affiliates or its sublicensees in connection with the Commercialization of a Product in the Territory.

1.144 "Product Regulatory Approval" means any Regulatory Documentation filed in the Territory which is related to a Product in the Licensed Field, whether in existence as of the Effective Date or filed with the applicable Regulatory Authority during the Term, including any supplements or amendments thereto.

1.145 "Product Trademarks" has the meaning set forth in Section 5.5(a).

1.146 "PVA" has the meaning set forth in Section 9.8(a)(i).

1.147 "Receiving Party" has the meaning set forth in Section 14.1.

1.148 "Regulatory Approval" means any approval or authorization, including Pricing Approvals, of any Regulatory Authority that is necessary for the Manufacture, use, storage, import, transport and/or sale of a Product in accordance with Applicable Laws.

1.149 "Regulatory Approval Application" means an NDA or BLA, or any corresponding application for Regulatory Approval in the Territory, including: (a) with respect to the European Union, an MAA filed with the EMA pursuant to the Centralized Approval Procedure or with the applicable Regulatory Authority of a country in Europe with respect to the decentralized procedure, mutual recognition or any national approval procedure; and (b) an MAA filed with the PMDA, including, in each case, all supplements, amendments, variations, extensions and renewals thereof.

1.150 "Regulatory Authority" means any applicable Governmental Authority involved in granting Regulatory Approval in a country or jurisdiction in the Territory, including in the U.S., the FDA and any other applicable Governmental Authority in the U.S. having jurisdiction over a Product; in the EU, the EMA or any competent Government Authority in the EU; in Japan, the PMDA; and any other applicable Governmental Authority having jurisdiction over a Product.

1.151 "Regulatory Documentation" means, with respect to each Research Product or Licensed Product, all: (a) Regulatory Materials, including all data contained therein and all supporting documents created for, submitted to or received from an applicable governmental agency or Regulatory Authority relating to such Regulatory Materials; and (b) other documentation or Information Controlled by a Party which is necessary or reasonably useful in order to Exploit such Product in the applicable Field in the Territory, including any registrations and licenses, regulatory drug lists, advertising and promotion documents shared with Regulatory Authorities, adverse event files, complaint files and Manufacturing records.

1.152 "Regulatory Exclusivity" means any exclusive marketing rights or data protection or other exclusivity rights conferred by any Regulatory Authority with respect to a Product in a country or jurisdiction in the Territory, other than a Patent right, including orphan drug exclusivity, pediatric exclusivity, rights conferred in the U.S. under the Hatch Waxman Act, in the EU under Directive 2001/83/EC, as amended, and Regulation (EC) No. 1901/2006, as amended, or in the Biologics Price Competition Act as set forth in the Patient Protection & Affordable Care Act, or rights similar thereto in other countries or regulatory jurisdictions in the Territory.

1.153 "Regulatory Materials" means, with respect to each Product, all documentation, correspondence, submissions and notifications submitted to or received from a Regulatory Authority that are necessary or reasonably useful in order to Exploit such Product in the applicable field in the Territory. For the avoidance of doubt, Regulatory Materials shall include, with respect to each Product, all INDs, Regulatory Approval Applications, Regulatory Approvals, Pricing Approvals and amendments and supplements for any of the foregoing, as well as the contents of any minutes from meetings (whether in person or by audio conference or videoconference) with a Regulatory Authority.

1.154 "Representative Expert" has the meaning set forth in Section 16.3(b).

1.155 "Research Materials" has the meaning set forth in Section 6.6(a).

1.156 "Research Plan" means a [***] Research Plan or Option Product Research Plan, as applicable.

1.157 "Research Product" means a [***] Product, Candidate Product or Option Product, as applicable.

1.158 "Research Support" has the meaning set forth in Section 7.1.

1.159 "Senior Officer" means the Head of Research & Development or his or her designee, in the case of Takeda and, the Chief Executive Officer or his or her designee, in the case of Ultragenyx.

1.160 "Takeda [***] License" means the licenses granted to Takeda in Section 3.2.

1.161 "Takeda Field" means [***].

1.162 "Takeda Indemnitee" has the meaning set forth in Section 17.1.

1.163 "Takeda Option" has the meaning set forth in Section 8.1.

1.164 "Takeda Option Field" means all human indications other than the Takeda Field for Licensed [***] Products, and all human indications for Licensed Analog Products, Licensed Option Products and Ultragenyx Pipeline Products.

1.165 "Takeda Option Negotiation Period" has the meaning set forth in Section 8.2(d).

1.166 "Takeda Option Notice" has the meaning set forth in Section 8.2(c).

1.167 "Takeda Option Term" means the period beginning on the Effective Date and ending on the earlier of (a) [***] after the Effective Date or (b) with respect to a Licensed [***] Product, Licensed Analog Product, Licensed Option Product, or Ultragenyx Pipeline Product, as

the case may be: (i) [***] after Takeda's receipt of the applicable Final Phase II Data Package for the applicable Licensed [***] Product, Licensed Analog Product or Licensed Option Product, (ii) [***] after Takeda's receipt of the Final Phase II Data Package (or Final Phase III Data Package in the case of [***]) for the applicable Ultragenyx Pipeline Product (other than [***]) and (iii) [***] after Takeda's receipt of the Final Phase II Data Package for [***]. Notwithstanding the foregoing, (a) in the event of a [***] of Ultragenyx [***], the Takeda Option Term will expire with respect to all applicable products (i.e., any Licensed [***] Product, Licensed Analog Product, Licensed Option Product, or Ultragenyx Pipeline Product) [***]; and (b) in the event of a [***] of Ultragenyx at any time [***], the Takeda Option Term will expire with respect to all applicable products (i.e., any Licensed [***] Product, Licensed Analog Product, Licensed Option Product, or Ultragenyx Pipeline Product) [***] after the closing of such [***].

1.168 "Takeda Patents" means the Licensed [***] Patent and any Patent that claims priority (in accordance with Section 1.129) to the Licensed [***] Patent during the Term, and the Ultragenyx Pipeline Improvement Patents Controlled by Takeda or its Affiliates. The Takeda Patents as of the Execution Date are set forth on Exhibit 1.168.

1.169 "Takeda Product Infringement" has the meaning set forth in Section 12.6(b)(i).

1.170 "Takeda ROFN Territory" means Japan.

1.171 "Takeda Royalty Term" means, on a country-by-country and Exercised Product-by- Exercised Product basis, the period commencing on the First Commercial Sale of such Exercised Product in a country in the Takeda Territory by Takeda, its Affiliates, or sublicensees that occurs after Takeda's exercise of the Takeda Option and ending upon the later of [***].

1.172 "Takeda Territory" means, (i) with respect to Licensed Products and Licensed Option Products, Japan and Asia and (ii) with respect Ultragenyx Pipeline Products, Japan.

1.173 "Tax Conditions" means, with respect to the premium being paid by Takeda to Ultragenyx under the Common Stock Purchase Agreement, Ultragenyx's confirmation of receipt of the tax residence certificate (IRS Form 6166) from the U.S. Internal Revenue Service specified in Section 11.11(c) and appropriate submission of such certificate and required forms and information with the Osaka Regional Taxation Bureau.

1.174 "Term" has the meaning set forth in Section 15.1.

1.175 "Terminated Product" means any: (a) Option Product for which an Option Product License Agreement has not been executed during the Option Negotiation Period in accordance with Section 6.12(a); (b) Research Product terminated pursuant to Section 6.7(d) or 18.5; (c) Licensed [***] Compound or Licensed [***] Product that reverts to Takeda pursuant to Section 4.3(f); or (d) Licensed Product or Research Product terminated pursuant to Section 15.2, 15.4 or 15.5.

1.176 "Territory" means worldwide.

1.177 "Third Party" means a Person other than Takeda and Ultragenyx and their respective Affiliates.

1.178 "Ultragenyx [***] Know-How" means all Information related to the Licensed [***] Compound Controlled by Ultragenyx during the Term.

1.179 "Ultragenyx [***] License" means the licenses granted to Ultragenyx in Section 3.1.

1.180 "Ultragenyx [***] Patents" means all Patents Controlled by Ultragenyx or its Affiliates as of the Execution Date or during the Term that are necessary or reasonably useful for the Exploitation of the Licensed [***] Compound or Licensed Analog Compound in the Licensed Field in the Territory, but expressly excluding any Licensed Product Improvement Patents. The Ultragenyx [***] Patents as of the Execution Date are set forth on Exhibit 1.188.

1.181 "Ultragenyx [***] Technology" means the Ultragenyx [***] Patents and Ultragenyx [***] Know-How.

1.182 "Ultragenyx Field" means the Licensed Field, excluding the Takeda Field.

1.183 "Ultragenyx In-License Agreement" means [***] and (g) any other applicable agreement between Ultragenyx (or its Affiliates) and a Third Party under which Takeda is granted a sublicense or other right under this Agreement.

1.184 "Ultragenyx Indemnitee" has the meaning set forth in Section 17.2.

1.185 "Ultragenyx Know-How" means all Information Controlled by Ultragenyx during the Term that is necessary or reasonably useful to Exploit a Compound or a Product in the Licensed Field.

1.186 "Ultragenyx Intellectual Property" means, collectively, Ultragenyx Know-How and Ultragenyx Patents.

1.187 "Ultragenyx Option" has the meaning set forth in Section 6.11.

1.188 "Ultragenyx Patents" means all Ultragenyx [***] Patents, Licensed Product Improvement Patents Controlled by Ultragenyx or its Affiliates, Option Product Improvement Patents Controlled by Ultragenyx or its Affiliates and Ultragenyx Pipeline Patents. The Ultragenyx Patents as of the Execution Date are set forth on Exhibit 1.188.

1.189 "Ultragenyx Pipeline Compound" means the active ingredient in an Ultragenyx Pipeline Product.

1.190 "Ultragenyx Pipeline Improvements" means any Invention related to an Ultragenyx Pipeline Product made (a) solely by, or on behalf of, Takeda or its Affiliates or sublicensees under this Agreement or (b) solely by Ultragenyx or its Affiliates under this Agreement. For clarity, (i) employees of Takeda or its Affiliates or sublicensees, or their respective agents or independent contractors receiving consideration from Takeda or its Affiliates or sublicensees in the course of conducting activities under this Agreement, shall be considered "solely by, or on behalf of" pursuant to this Section 1.190, and (ii) neither Ultragenyx nor any of its Affiliates shall, under any circumstances under this Agreement, be considered an agent or independent contractor of Takeda or any of its Affiliates or sublicensees for purposes of this Section 1.190.

1.191 "Ultragenyx Pipeline Improvement Patents" means Patents that Cover Ultragenyx Pipeline Improvements.

1.192 "Ultragenyx Pipeline Patents" means all Patents Controlled by Ultragenyx as of the Execution Date and during the Term that: (a) claim the composition of matter of, or the method of making or using an Ultragenyx Pipeline Product; or (b) are otherwise necessary or reasonably useful to Exploit an Ultragenyx Pipeline Product in the Licensed Field. The Ultragenyx Pipeline Patents for the Takeda Territory as of the Execution Date are set forth on Exhibit 1.188.

1.193 "Ultragenyx Pipeline Products" means all products that have entered into Clinical Trials and are Controlled by Ultragenyx or its Affiliates during the Collaboration Term and that Ultragenyx or its Affiliates have rights to Commercialize in the Takeda ROFN Territory, [***]. For purposes of this Section 1.193, "Controlled" shall not include [***]

[***].

1.194 "Ultragenyx Product Infringement" has the meaning set forth in Section 12.6(b)(i).

1.195 "UX[***]" means the compound having Ultragenyx reference number UX[***] as further described on Exhibit 1.195.

1.196 "UX[***]" means the compound having Ultragenyx reference number UX[***] as further described on Exhibit 1.195.

1.197 "UX[***]" means the compound having Ultragenyx reference number UX[***] as further described on Exhibit 1.195.

1.198 "UX[***]" means the compound having Ultragenyx reference number UX[***] as further described on Exhibit 1.195.

1.199 "UX[***]" means the compound having Ultragenyx reference number UX[***] as further described on Exhibit 1.195.

1.200 "Valid Claim" means a claim of an issued and unexpired Patent included within the Takeda Patents, the Ultragenyx Patents or the Joint Patents, to the extent such claim has not been revoked, held invalid or unenforceable by a patent office, court or other governmental agency of competent jurisdiction in a final order, from which no further appeal can be taken, and which claim has not been disclaimed, denied or admitted to be invalid or unenforceable through reissue, re-examination or disclaimer.

1.201 "Validation Research Plan" has the meaning set forth in Section 6.2(b).

ARTICLE 2 – OVERVIEW; MANAGEMENT

2.1 Joint Steering Committee for Licensed Products.

(a) **Formation and Purpose**. Within thirty (30) days after the Effective Date, the Parties shall promptly establish and convene a Joint Steering Committee (the "Joint Steering Committee" or "JSC") in accordance with Section 2.3(c)(i) that will direct and oversee activities relating to the Licensed Products under this Agreement. The JSC shall consist of representatives and operate by the procedures in accordance with Section 2.3. Except as otherwise provided herein, the role of the Joint Steering Committee shall be:

(i) to encourage and facilitate ongoing communication and cooperation between the Parties with respect to the Exploitation by the Parties of Licensed Products in the Licensed Field;

(ii) to serve as a forum for sharing discoveries and exchanging data and results generated by each Party relating to additional compounds Covered by the Licensed [***] Patent;

(iii) to evaluate and approve the inclusion as Licensed Analog Compounds of additional compounds that are Covered by the Licensed [***] Patent but that do not meet the definition of Licensed Analog Compounds [***];

(iv) to evaluate and approve the exclusion from the definition of Licensed Analog Compounds of additional compounds that are Covered by the Licensed [***] Patent [***];

(v) to review and discuss [***] Development Plans and any proposed amendments or revisions to the [***] Development Plans;

(vi) to review and discuss Commercialization Plans including the review and discussion of any amendments to such Commercialization Plans;

(vii) to review and discuss Licensed Product regulatory issues, including those raised by the joint regulatory affairs working group established pursuant to Section 2.1(a)(viii) and Section 9.4(a);

(viii) to establish other such working groups or subcommittees, as needed to further the purposes of the Agreement relating to Licensed Products, as mutually agreed by the Parties in writing;

(ix) to resolve any disputes referred to the JSC; and

(x) to approve or decide such other matters as provided in this Agreement.

(b) **JSC Decisions; Final Decision Authority.**

(i) The JSC will make good faith efforts to make all decisions by consensus. Except as set forth in Section 2.1(b)(ii), actions to be taken by the Joint Steering Committee shall be taken only following unanimous vote, with each Party's representatives collectively having one (1) vote. If the Joint Steering Committee fails to reach unanimous agreement on a matter before it for decision for a period in excess of fifteen (15) days from the date first presented to the JSC in writing, either Party may submit such matter for resolution to the Senior Officers of the Parties for attempted resolution by good faith negotiation within thirty (30) days after such notice is received by the Senior Officers.

(ii) If the Senior Officers of the Parties are unable to resolve such dispute within such thirty (30) day period, such dispute shall be resolved during the Term as follows. For the avoidance of doubt, the right of a Party to make final decisions with respect to any issue

shall not otherwise diminish or eliminate such Party's obligations under this Agreement, including its obligation to exercise Commercially Reasonable Efforts where required herein.

(A) Subject to Sections 2.1(b)(ii)(D) and 2.1(b)(ii)(E) and provided that such decision does not result in an increase in the scope of work or costs associated with the performance of any activities by Takeda under this Agreement, Ultragenyx will have final decision making authority over [***]; and

(B) Takeda will have final decision making authority over [***].

(C) Takeda will have final decision making authority over [***].

(D) If Ultragenyx exercises the [***] Option within the [***] Option Term for the co-Development and co-Commercialization of Licensed [***] Products in the Takeda Field in the Territory, Takeda will have final decision making authority over [***].

(E) If Ultragenyx does not exercise the [***] Option within the [***] Option Term for the co-Development and co-Commercialization of Licensed [***] Products in the Takeda Field in the Territory, (a) Ultragenyx will continue to have final decision making authority over [***], and (b) Takeda will continue to have final decision making authority over [***].

(F) Takeda shall have final decision making authority over [***];

(G) Ultragenyx shall have final decision making authority over [***].

(iii) Neither Party shall have the final decision making authority for any other matter under the purview of the JSC and not covered by subsections (A)-(G), and the status quo shall persist with respect to such matter if the Parties are unable to agree. For clarity, the Parties anticipate that Licensed Option Products and Exercised Products will be governed by separate committees and final decision making authority to be established pursuant to the applicable Option Product License Agreement or Exercised Product License Agreement, respectively.

(c) **Discontinuation of JSC.** Upon [***] or any time thereafter, Ultragenyx shall have the right, upon written notice to Takeda, to

discontinue its participation in the JSC. Once Ultragenyx has provided such notice to Takeda, the JSC shall have no further obligations under this Agreement and, thereafter, Takeda shall have final decision making authority with respect to the topics that were otherwise determined by the JSC, subject to the other terms and conditions of this Agreement.

2.2 **Joint Research Committee for Collaboration Activities**.

(a) **Formation and Purpose**. Within thirty (30) days after the Effective Date, the Parties shall promptly establish and convene a Joint Research Committee (the "Joint Research Committee" or "JRC") in accordance with Section 2.3(c)(i) for the overall coordination and oversight of the Collaboration Activities. The JRC shall consist of representatives and operate by the procedures in accordance with Section 2.3. Except as otherwise provided herein, the Joint Research Committee shall be responsible for supporting the [***] in assessing, prioritizing, and advancing Takeda's rare genetic disease products, including the following specific activities (collectively, "Collaboration Activities"):

(i) review and approve the Validation Research Plan and any amendments thereto;

(ii) review and approve the Option Product Research Plans and any amendments thereto;

(iii) review and approve any amendments to the [***] Research Plan;

(iv) evaluate and prioritize [***];

(v) support the overall direction of Candidate Product and Option Product strategy;

(vi) identify, define, and support collaborations with key experts and investigators and other third parties in support of the prioritized Candidate Products, Option Products and related indications;

(vii) identify and implement opportunities [***];

(viii) determine the [***]; and

(ix) oversee and manage the secondee program provided for in Section 2.6.

(b) **Termination of Responsibilities.** Upon execution of an Option Product License Agreement for an Option Product, the JRC will no longer have any responsibility over or decision making authority relating to such Option Product.

(c) **JRC Decisions; Final Decision Authority**.

(i) The JRC will make good faith efforts to make all decisions by consensus Except as set forth in Section 2.2(c)(ii), actions to be taken by the Joint Research Committee shall be taken only following unanimous vote, with each Party's representatives collectively having one (1) vote. If the Joint Research Committee fails to reach unanimous agreement on a matter before it for decision for a period in excess of fifteen (15) days from the date first presented to the JRC in writing, either Party may submit such matter for resolution to the Senior Officers of the Parties for attempted resolution by good faith negotiation within thirty (30) days after such notice is received among the Senior Officers.

(ii) If the Senior Officers of the Parties are unable to resolve such dispute within such thirty (30) day period, such dispute shall be resolved during the Collaboration Term as follows. For the avoidance of doubt, the right of a Party to make final decisions with respect to any issue shall not otherwise diminish or eliminate such Party's obligations under this Agreement, including its obligation to exercise Commercially Reasonable Efforts where required herein.

(A) Ultragenyx will have final decision making authority over [***];

(B) The Parties must mutually agree on the scope of Research Support to be provided by Takeda. If the Parties are unable to unanimously agree on the scope of the Research Support to be provided, then no Research Support shall be provided;

(C) Takeda will have final decision making authority over [***]; and

(D) Neither Party shall have the final decision making authority for any other matter under the purview of the JRC and not covered by subsections (A)-(C), and the status quo shall persist with respect to such matter if the Parties are unable to agree. For clarity, the Parties anticipate that Licensed Option Products will be governed by a separate committee and final decision making authority to be established pursuant to the Option Product License Agreement.

2.3 **Committee Membership and Procedures**.

(a) **Membership.** Takeda and Ultragenyx shall each designate an equal number of representatives to serve on the JSC and the JRC (each, a "Committee") by written notices to the other Party. Promptly after the Effective Date, each Party shall designate three (3)

representatives for the JSC and three (3) representatives for the JRC. Each Committee may elect to vary the number of representatives from time to time during the Term; provided that each Committee shall maintain an equal number of representatives from each Party. Each representative shall have the appropriate level of experience in the subject area of the Committee, and at least one (1) representative shall have sufficient seniority within the applicable Party's organization to have the necessary decision-making authority in order for the Committee to fulfill its responsibilities. Either Party may designate substitutes for its Committee representatives if one (1) or more of such Party's designated representatives is unable to be present at a meeting. From time to time each Party may replace its Committee representatives by written notice to the other Party specifying the prior representative(s) and their replacement(s).

(b) **Chairperson**. Each Committee will have two chairpersons, one designated by each of the Parties. The chairpersons shall be responsible for calling and convening meetings, but shall have no special authority over the other members of the Committee, and shall have no additional voting rights. The chairpersons (or their designates) shall jointly: (i) prepare and circulate an agenda reasonably in advance of each upcoming meeting; and (ii) prepare and issue minutes of each Committee meeting within thirty (30) days thereafter. Such minutes shall not be finalized until each Committee representative reviews and approves such minutes in writing; provided that any minutes shall be deemed approved unless a member of such Committee objects to the accuracy of such minutes within fifteen (15) days after the circulation of the minutes.

(c) **Meetings**.

(i) **Committee Meetings.** Each Committee shall meet at least once each Calendar Quarter. Additional meetings of the Committees may be held with the consent of each Party (such consent not to be unreasonably withheld, conditioned or delayed), as required under this Agreement. In the case of any dispute referred to a Committee, such meeting shall be held within five (5) Business Days following referral to the Committee, or as soon as reasonably possible.

(ii) **General Requirements.** Meetings of a Committee shall be effective only if a majority of representatives of each Party are present or participating. Other than the initial meeting, which shall be held in person, a Committee may meet either (A) in person at either Party's facilities or at such locations as the Parties may otherwise agree; or (B) by audio or video teleconference. Additional non-members of a Committee having relevant experience may from time to time be invited to participate in a Committee meeting, provided that such participants shall have no voting rights or powers. Non-member participants who are not employees of a Party or its Affiliates shall only be allowed to attend if: (i) the other Party's representatives have consented to the attendance (such consent not to be unreasonably withheld, conditioned or delayed); and (ii) such non-member participant is subject to confidentiality and non-use obligations at least as restrictive as those set forth in this Agreement. Each Party shall be responsible for all of its own expenses incurred in connection with participating in the Committees including all travel and all expenses associated with an initial alliance kick-off meeting. All other expenses incurred by a Committee in furtherance of a meeting, such as expenses associated with off-site meetings, shall be shared equally by the Parties.

2.4 **Alliance Managers**. Promptly following the Effective Date, each Party shall designate in writing an Alliance Manager to serve as the primary point of contact for the Parties regarding all collaboration and transition activities contemplated under this Agreement. Each Alliance Manager shall facilitate communication and coordination of the Parties' activities under this Agreement relating to the Products and shall plan the Committee meetings. The Alliance Managers shall be allowed to attend Committee meetings as non-voting observers.

2.5 **Authority**. The Parties agree that, in voting on matters as described in this ARTICLE 2, it shall be conclusively presumed that unless otherwise explicitly stated, each voting member of a Committee has the authority and approval of such member's respective senior management in casting his or her vote. Each Committee shall have only the powers assigned expressly to it in this ARTICLE 2 and elsewhere in this Agreement, and shall not have any power to amend, modify or waive compliance with this Agreement.

2.6 **Takeda Secondee.** Takeda shall have the right, at its own expense, to place one employee of Takeda or its Affiliates, who is reasonably acceptable to Ultragenyx, as a secondee with Ultragenyx at any time during the Collaboration Term; provided that such secondee shall enter into a confidentiality agreement with Ultragenyx prior to placement. Takeda may, one or more times during the Collaboration Term, substitute such employee with another employee of Takeda or its Affiliates.

ARTICLE 3 – LICENSES FOR [***] AND ANALOGS

3.1 **Licenses from Takeda to Ultragenyx.** Subject to the terms and conditions of this Agreement, Takeda hereby grants to Ultragenyx in the Territory during the Term:

(a) an exclusive (even as to Takeda and its Affiliates, subject to the retention of rights to conduct activities under the [***] Development Plan) license, with the right to grant sublicenses solely in accordance with Section 3.3, under the Licensed [***] Technology, Licensed Product Improvements Controlled by Takeda or its Affiliates, Licensed Product Improvement Patents Controlled by Takeda or its Affiliates, and Joint Intellectual Property to Exploit the Licensed [***] Products in the Ultragenyx Field;

(b) a co-exclusive license, without the right to grant sublicenses, under the Licensed [***] Technology, Licensed Product Improvements Controlled by Takeda or its Affiliates, Licensed Product Improvement Patents Controlled by Takeda or its Affiliates, and Joint Intellectual Property to conduct activities under the [***] Development Plan in the Takeda Field in the Territory; and

(c) an exclusive (even as to Takeda and its Affiliates) license, including the right to grant sublicenses solely in accordance with Section 3.3, under the Licensed [***] Technology, Licensed Product Improvements Controlled by Takeda or its Affiliates, Licensed Product Improvement Patents Controlled by Takeda or its Affiliates, and Joint Intellectual Property to Exploit the Licensed Analog Compounds and Licensed Analog Products in the Licensed Field in the Territory; provided, however, that, notwithstanding the licenses granted in this Section 3.1(c), at any time during the Term Ultragenyx shall not, and shall cause its Affiliates not to (i)

directly or indirectly Exploit any Licensed Analog Product in the Takeda Field or (ii) license, authorize, appoint, or otherwise enable any Third Party to, directly or indirectly, Exploit any Licensed Analog Product in the Takeda Field.

3.2 **Licenses from Ultragenyx to Takeda.** Subject to the terms and conditions of this Agreement, Ultragenyx hereby grants to Takeda in the Territory during the Term:

(a) an exclusive (even as to Ultragenyx and its Affiliates, subject to the retention of rights to conduct activities under the [***] Development Plan) license, with the right to grant sublicenses under multiple tiers solely in accordance with Section 3.3, under the Ultragenyx [***] Technology**,** Licensed Product Improvements Controlled by Ultragenyx or its Affiliates, Licensed Product Improvement Patents Controlled by Ultragenyx or its Affiliates, and Joint Intellectual Property to (i) Exploit the Licensed [***] Products in the Takeda Field in the Territory, and (ii) Exploit any structures Covered by the Licensed [***] Patent, other than with respect to Licensed Analog Compounds, in the Takeda Field in the Territory.

(b) a co-exclusive license, without the right to grant sublicenses, under the Ultragenyx [***] Technology**,** Licensed Product Improvements Controlled by Ultragenyx or its Affiliates, Licensed Product Improvement Patents Controlled by Ultragenyx or its Affiliates, and Joint Intellectual Property to conduct activities under the [***] Development Plan in the Ultragenyx Field in the Territory and to perform the activities under the [***] Development Plan.

3.3 **Sublicensing**. Each Party shall have the right to grant sublicenses, through multiple tiers, of the rights granted to such Party under Sections 3.1(a) and 3.1(c) (in the case of Ultragenyx) and Section 3.2(a) (in the case of Takeda), to its Affiliates and to Third Parties; provided, however that (a) subject to Section 5.2, Ultragenyx shall not grant a sublicense of the rights granted to it under (i) Section 3.1(a) to a Third Party without the prior written consent of Takeda (not to be unreasonably withheld, conditioned or delayed) or (ii) Section 3.1(c) in the Takeda Field and (b) Takeda shall not grant a sublicense of the rights granted to it under Section 3.2(a) to a Third Party without the prior written consent of Ultragenyx (not to be unreasonably withheld, conditioned or delayed). Each sublicense shall refer to and be subordinate to this Agreement and, except to the extent the Parties otherwise agree in writing, any sublicense must be consistent in all material respects with the terms and conditions of this Agreement. Upon termination of this Agreement, any sublicense granted by Ultragenyx to a Third Party shall continue and be transferred to Takeda and any sublicense granted by Takeda to a Third Party shall continue and be transferred to Ultragenyx; provided that such sublicenses comply with the requirements of this Section 3.3. Each Party shall remain responsible for the performance of this Agreement and the performance of its sublicensees hereunder.

3.4 **No Implied Licenses**. No license or other right is or shall be created or granted hereunder by implication, estoppel, or otherwise. All licenses and rights are or shall be granted only as expressly provided in this Agreement. All rights not expressly granted by a Party under this Agreement are reserved by the Party and may not be used by the other Party for any purpose.

ARTICLE 4 – LICENSED PRODUCT DEVELOPMENT

4.1 **Overview of Product Development**. The Parties desire and intend to collaborate with respect to the Development of the Licensed Product in the Licensed Field in the Territory, to the extent set forth in this Agreement. Takeda's Development of the Licensed [***] Products in the Takeda Field and Ultragenyx's Development of the Licensed [***] Products in the Ultragenyx Field and Licensed Analog Products in the Licensed Field shall be conducted in a manner consistent with the [***] Development Plans and using Commercially Reasonable Efforts.

4.2 **Transition and Exchange of Know-How**

(a) **Transition from Takeda to Ultragenyx.** As soon as practicable after the Effective Date, the Parties will cooperate and act in good faith to support the transition of the Licensed [***] Product from Takeda to Ultragenyx in the Ultragenyx Field and, solely for purposes of Ultragenyx's performance of its obligations under Section 4.3(a)(ii), in the Takeda Field, at no additional consideration payable to Takeda, including the (i) transition and, to the extent appropriate, assignment of Regulatory Materials and Regulatory Approvals covering the Licensed [***] Product in the Ultragenyx Field and, solely for purposes of Ultragenyx's performance of its obligations under Section 4.3(a)(ii), in the Takeda Field, from Takeda to Ultragenyx, (ii) sharing of the Licensed [***] Know-How with Ultragenyx to the extent necessary or reasonably useful for the use of the Licensed [***] Product and the Licensed Analog Products for and implementation of the Initial [***] Development Plan, and (iii) transferring to Ultragenyx, at no cost to Ultragenyx, those biological materials or chemical compounds related to the Licensed [***] Product Controlled by Takeda as of the Execution Date as are necessary for Ultragenyx to perform the activities allocated to it under the Initial [***] Development Plan. Takeda will also use Commercially Reasonable Efforts, at Ultragenyx's sole cost and expense, to assign or sublicense to Ultragenyx any existing Third Party agreements that are necessary or reasonably useful for the Exploitation of a Licensed [***] Product in the Ultragenyx Field in the Territory. Within forty-five (45) days after the receipt of an invoice from Takeda reflecting the costs and expenses of such assignment or sublicense, Ultragenyx shall pay the invoiced amounts to Takeda.

(b) **Know-How Sharing by Ultragenyx.** Ultragenyx shall provide to Takeda, promptly after the Effective Date and during the Term upon Ultragenyx Know-How being obtained or generated by Ultragenyx, at no additional cost or expense to Takeda, all such Ultragenyx Know-How as is necessary or reasonably useful to enable Takeda: (a) to perform its obligations under this Agreement; (b) to Exploit the Licensed [***] Product in the Takeda Field, and (c) to Exploit any structures Covered by the Licensed [***] Patent, other than with respect to Licensed Analog Compounds, in the Takeda Field in the Territory.

4.3 **Development Activities**.

(a) Throughout the Term, Ultragenyx will use Commercially Reasonable Efforts to (i) Exploit a Licensed [***] Product or Licensed Analog Product in the Ultragenyx Field in the Territory and (ii) complete Development activities for a Licensed [***] Product in the Takeda

Field, in each case at Ultragenyx's sole expense and pursuant to the Initial [***] Development Plan.

(b) If the Parties mutually agree to conduct other Development activities with respect to a Licensed [***] Product other than as set forth in the Initial [***] Development Plan, then the Parties shall prepare a plan (including timeline and budget) covering the Development activities to be completed, the Party responsible for completing such activities, and the Party responsible for the associated costs (together with the Initial [***] Development Plan, the "[***] Development Plans").

(c) If Ultragenyx elects to pursue Development of a Licensed Analog Product, Ultragenyx will use Commercially Reasonable Efforts to Exploit such Licensed Analog Product in the Ultragenyx Field in the Territory at Ultragenyx's sole expense and pursuant to a [***] Development Plan for such Licensed Analog Product.

(d) At Ultragenyx's sole expense, Takeda, using Commercially Reasonable Efforts, will (i) conduct initial manufacturing process development and scale-up activities for the Licensed Products as set forth in the Initial [***] Development Plan and in accordance with the agreed upon budget contained therein, (ii) will work with Ultragenyx to transfer Licensed [***] Know-How as necessary or reasonably useful for Development and for the purposes of completing Regulatory Applications, initiating Clinical Trials and for transitioning manufacturing activities to Ultragenyx, and (iii) conduct such other Development and Manufacturing activities as may be mutually agreed by the Parties.

(e) Each Party shall conduct its activities under this Agreement in good scientific manner and in compliance in all material respects with all Applicable Laws, including, GCP, GLP, and GMP.

(f) If Ultragenyx breaches its obligations under Section 4.3(a) or 4.3(c) or is otherwise no longer actively conducting Development of a Licensed [***] Compound and Licensed [***] Product in any indication in the Ultragenyx Field, then [***] of the date Ultragenyx stopped actively conducting such Development, the Ultragenyx [***] License for the Licensed [***] Compound and Licensed [***] Product shall terminate and, [***] of such event, such license shall revert to Takeda and the terms of Section 15.7(c) shall apply with respect to such Compound and Product; provided, that, upon the reversion of rights to Takeda, Takeda shall not develop such Product in the Ultragenyx Field except in accordance with Takeda's exercise of the Takeda Option or right of first negotiation pursuant to ARTICLE 8. If, prior to the effective date of such reversion, Ultragenyx determines it wishes to license such Compound or Product from Takeda in the Ultragenyx Field, Ultragenyx may provide written notice to Takeda. Following receipt of such notice, Takeda and Ultragenyx will negotiate in good faith such license agreement for a period of [***] thereafter, which period may be extended by mutual agreement. Any resulting license agreement will be subject to Takeda's exercise of the Takeda Option or right of first negotiation pursuant to ARTICLE 8.

(g) Neither Party may Develop Licensed [***] Products in the Ultragenyx Field except as set forth in the [***] Development Plan. Takeda shall have the sole discretion to Develop Licensed [***] Products in the Takeda Field.

4.4 **Clinical Trial Registry**.

(a) Ultragenyx shall be responsible for registering any Clinical Trial performed pursuant to the [***] Development Plans in the appropriate clinical trial registry (e.g., clinicaltrials.gov) and posting the results of such Clinical Trials as required by Applicable Laws.

(b) The posting of any results to a clinical trial registry in accordance with this Section 4.4 shall be considered a "publication" and subject to the Parties' obligations set forth in Section 14.9.

4.5 **Records; Disclosure of Data and Results.** In conformity with standard pharmaceutical industry practices and the terms and conditions of this Agreement, each Party shall prepare and maintain, or shall cause to be prepared and maintained, complete and accurate written records, accounts, notes, reports and data with respect to activities conducted pursuant to the [***] Development Plans for a minimum of three (3) years following the end of the Calendar Year to which they pertain (or such longer period as may be required by Applicable Laws) and, upon the other Party's reasonable written request, shall send legible copies (in English and in electronic format) of the aforesaid to the other Party, to the extent not already provided, throughout the Term and for a minimum of twelve (12) months following the Term. Upon reasonable advance notice, at the request of the JSC, each Party agrees to make its employees and consultants reasonably available at their respective places of employment to consult with the other Party on issues arising in connection with the [***] Development Plans. In accordance with the reporting format and schedule approved by the JSC, each Party shall promptly and fully disclose to the other Party in writing all data, including preclinical data, Clinical Trial data, formulation data and manufacturing data, generated by or on behalf of such Party with respect to the Products in the Licensed Field. Without limiting the foregoing: (a) Ultragenyx shall keep Takeda regularly and fully informed by reporting to the JSC on a quarterly basis regarding the Development of Licensed Products in the Ultragenyx Field in the Territory by Ultragenyx, its Affiliates and sublicensees, including information regarding the status of Clinical Trials, filing of Regulatory Materials and receipt of Regulatory Approval with respect to the Products in the Ultragenyx Field in the Territory; (b) on at least an annual basis (but in any event, no later than December 1 of each Calendar Year), each Party, as applicable, shall submit to the JSC proposed updates and amendments, as appropriate, to the [***] Development Plans; and (c) Takeda shall keep Ultragenyx regularly informed by reporting to the JSC on a quarterly basis regarding the Development of Licensed Products in the Takeda Field by Takeda, its Affiliates and sublicensees, including information regarding the status of any Clinical Trials, filing of Regulatory Materials and receipt of Regulatory Approval with respect to the Products in the Takeda Field in the Territory.

ARTICLE 5– [***] CO-DEVELOPMENT AND CO-COMMERCIALIZATION

5.1 **Co-Development and Co-Commercialization Negotiation for Takeda Field**.

(a) As soon as practicable, but no later than [***], Ultragenyx shall deliver to Takeda the Final [***] Data Package for such Licensed Product. For a period of [***] following the deadline for delivery of such Final [***] Data Package for the first Licensed [***] Product or Takeda's earlier receipt of such Final [***] Data Package (the "[***] Option Term"), Ultragenyx will have the right to exercise an exclusive option to co-Develop and co-Commercialize the Licensed [***] Products in the Takeda Field in the Territory (the "[***] Option"). Upon exercise of the [***] Option prior to the expiration of the [***] Option Term, the Parties will negotiate in good faith, for a period of up to [***] (the "[***] License Negotiation Period"), the terms relating to the co-Development and co-Commercialization of the Licensed [***] Products in the Takeda Field in the Territory (other than the rights regarding final decision making authority of the Parties, which will be as set forth in Section 2.1(b)(ii)(D)).

(b) If Ultragenyx exercises the [***] Option within the [***] Option Term and the Parties reach agreement regarding the co-Development and co-Commercialization of the Licensed [***] Product in the Takeda Field within the [***] License Negotiation Period, such agreement, including any needed modification to the Ultragenyx [***] License and Takeda [***] License, will be entered into by the Parties or their designated Affiliates. Such agreement shall provide that, if Ultragenyx terminates the Development of Licensed [***] Products in the Ultragenyx Field, then Ultragenyx shall have the right to terminate such co-Development and co- Commercialization of Licensed [***] Products in the Takeda Field upon providing Takeda with the following prior written notice: (i) if the Licensed [***] Product is in Development at the time of termination, [***], and (ii) if the Licensed [***] Product is being Commercialized at the time of termination, [***].

(c) If Ultragenyx exercises the [***] Option within the [***] Option Term and the Parties fail to reach an agreement regarding the co-Development and co-Commercialization of the Licensed [***] Product in the Takeda Field within the [***] License Negotiation Period, then Takeda and Ultragenyx shall have the right to submit their proposed terms for such co- Development and co-Commercialization of the Licensed [***] Products in the Takeda Field in the Territory to binding arbitration as set forth in Section 16.3; provided, however, that the rights regarding the final decision making authority of the Parties as set forth in Section 2.1(b)(ii)(D) will not be subject to modification in such arbitration.

5.2 **Takeda Right of First Negotiation for the Ultragenyx Field.** Notwithstanding Ultragenyx's right to sublicense under Section 3.3, Ultragenyx does not have the right to enter into an agreement with any Third Party for the co-Development and/or co-Commercialization (including co-promotion) of the Licensed Product in the Ultragenyx Field except in accordance with the terms of this Section 5.2. If Ultragenyx intends to co-Develop and/or co-Commercialize (including co-promote) with a Third Party a Licensed Product in the Ultragenyx Field, Ultragenyx will provide Takeda with prior written notice of such intent and, for a period of [***] after receipt of such notice, Takeda will have a right of first negotiation to enter into a definitive agreement with Ultragenyx for such co-Development and/or co-Commercialization (including co-promotion). If the Parties fail to enter into a definitive

agreement prior to the expiration of [***], Ultragenyx will have the right to enter into a definitive agreement with a Third Party (including via sublicensing as set forth in Section 3.3) for the co-Development and/or co-Commercialization (including co- promotion) of the Licensed Product in the Ultragenyx Field; provided, that, [***], Ultragenyx shall not enter into such a definitive agreement with a Third Party on terms, when viewed as a whole, that are less favorable to Ultragenyx than the terms last offered to Ultragenyx by Takeda.

5.3 **Commercialization Plans.** Each Party shall submit a Commercialization Plan to the JSC for discussion no less [***] prior to the anticipated date of such Party obtaining Regulatory Approval for a Licensed Product. Thereafter, each Party shall provide a copy of the then-current Commercialization Plan to the JSC at least once each Calendar Year during the Licensed Product Royalty Term and Takeda Royalty Term, as applicable.

5.4 **Commercialization Activities.**

(a) **Ultragenyx Commercialization**. Ultragenyx shall use Commercially Reasonable Efforts to Commercialize the Licensed Product in the Ultragenyx Field in the Territory throughout the Term. Subject to any modifications based on agreements reached pursuant to Sections 5.1 and 5.2, Ultragenyx's Commercially Reasonable Efforts requirements and the provisions of Section 2.1(b), Ultragenyx has sole discretion relating to all aspects of the Commercialization of Licensed Products in the Ultragenyx Field in the Territory. As between the Parties, Ultragenyx shall bear all of the costs and expenses incurred in connection with all such Commercialization activities. On an annual basis, and no later than March 1 of each Calendar Year following the First Commercial Sale of a Licensed Product in the Ultragenyx Field in the Territory, Ultragenyx shall present a reasonably detailed written report to the JSC summarizing Ultragenyx's overall Commercialization activities undertaken during the previous Calendar Year with respect to the Licensed Products in the Ultragenyx Field.

(b) **Takeda Commercialization**. Subject to any modifications based on agreements reached pursuant to Sections 5.1 and 5.2 and the provisions of Section 2.1(b), Takeda has sole discretion relating to the Commercialization of Licensed [***] Products in the Takeda Field in the Territory. As between the Parties, Takeda shall bear all of the costs and expenses incurred in connection with all such Commercialization activities.

5.5 **Trademarks**.

(a) **Ownership.** Each Party shall own, throughout the world, each Product trademark that it develops for a Product in its Field in the Territory (each a "Product Trademark"). All goodwill attributable to a Party's Product Trademark generated by the Commercialization of a Product bearing such mark shall inure to the benefit of such Party.

(b) **Use.** Neither Party shall be obligated to use the other Party's Product Trademark or House Marks except to the extent required by Applicable Law or regulatory requirement. Neither Party shall, during the Term or thereafter, adopt, register or use any trademark, trade

name, brand name, symbol or logo that is identical, or confusingly similar, to the other Party's Product Trademarks.

(c) **Filing; Maintenance.** Each Party shall solely be responsible for, and shall solely bear all costs associated with maintenance and enforcement of, such Party's Product Trademark.

ARTICLE 6 – RESEARCH COLLABORATION

6.1 **Research Collaboration Generally**. The Parties will conduct research of Takeda's [***] Compound and Candidate Products as set forth in this Agreement. As further described below, the Candidate Products will be selected from the Takeda-Controlled compounds listed on Exhibit 6.1 attached hereto, as may be amended from time to time by Takeda in its sole discretion (the "Listed Compounds").

6.2 **Nomination of Candidate Products and Validation Research**.

(a) **Nomination**. Either Party may nominate compounds from the Listed Compounds for consideration and approval by the JRC as candidate products under this Agreement (upon such approval, each such Listed Compound shall thereafter be a "Candidate Product"). The JRC may select up to five (5) Candidate Products for validation pursuant to Section 6.2(b) at any one time. If five (5) Candidate Products have been selected at any one time, neither Party may nominate any additional Listed Compound to be considered as a Candidate Product unless and until the Parties determine, after the completion or termination of research activities under the applicable Validation Research Plan, that a Candidate Product will not be nominated as an Option Product.

(b) **Validation Research Plan**. Takeda will design, with input from Ultragenyx, a research plan and budget for the initial validation for each Candidate Product (each, a "Validation Research Plan"), with each such Validation Research Plan intended to sufficiently include the activities required to provide information and data necessary for the JRC to determine whether to nominate a Candidate Product as an Option Product. Each Validation Research Plan will be submitted to the JRC for approval (for which Takeda will have final decision-making authority in accordance with Section 2(c)(ii)(C)) and will be funded by Takeda and performed by or on behalf of Takeda, in Takeda's sole discretion.

6.3 **[***] Research Plan and Transition**

(a) During the Collaboration Term with respect to the [***] Products, the Parties will use Commercially Reasonable Efforts to Exploit the [***] Products, at Ultragenyx's sole expense, pursuant to the initial research plan and budget for the [***] Products attached hereto as Exhibit 6.3(a) (the "[***] Research Plan"). Pursuant to the [***] Research Plan and in accordance with the associated budget, at Ultragenyx's sole expense, Takeda will use Commercially Reasonable Efforts to conduct initial Manufacturing process development and scale-up of the [***] Products, as agreed by the Parties. For clarity, there will not be any Validation Research Plan for the [***] Products.

(b) During the Collaboration Term with respect to the [***] Products, the Parties shall cooperate and act in good faith to support the transition of the [***] Products from Takeda to Ultragenyx in the Licensed Field to the extent necessary or reasonably useful for Ultragenyx to perform the [***] Research Plan, including the transition of Option Product Know-How with respect to the [***] Products. [***].

6.4 **Option Product Research Plan**. During the Collaboration Term with respect to each Option Product for which there is an agreed Option Product Research Plan, Ultragenyx will use Commercially Reasonable Efforts to Exploit each Option Product in accordance with the applicable Option Product Research Plan.

6.5 **Limited Licenses During the Collaboration Term**.

(a) **License to Ultragenyx**.

(i) Upon selection of a Candidate Product as an Option Product by the JRC and as of the Effective Date with respect to [***] Products, Takeda hereby grants to Ultragenyx a limited, co-exclusive (with Takeda and its Affiliates), non-transferable, non-sublicensable, royalty-free license under the Option Product Technology, Option Product Improvements Controlled by Takeda or its Affiliates, Option Product Improvement Patents Controlled by Takeda or its Affiliates, and Joint Intellectual Property to Exploit the Option Product solely in accordance with the activities to be performed by Ultragenyx under the Option Product Research Plan.

(ii) The foregoing license under Section 6.5(a)(i) will continue on an Option Product-by-Option Product basis until the earlier of (A) execution of an Option Product License Agreement, (B) failure by the Parties to enter into an Option Product License Agreement by the expiration of the applicable Option Negotiation Period, or (C) expiration or termination of the Collaboration Term, at which time such Option Product shall be a Terminated Product and all rights to such Option Product will revert to Takeda in accordance with Section 15.7(c); provided that, if in the case of (C), an Option Negotiation Period is then ongoing, the Collaboration Term with respect to such Option Product will automatically extend until the earlier of (1) expiration of such Option Negotiation Period or (2) execution of the applicable Option Product License Agreement.

(b) **License to Takeda**. During the Collaboration Term, with respect to each Research Product, Ultragenyx hereby grants to Takeda a limited, non-exclusive, non- transferable, non-sublicensable, royalty-free license, under all Ultragenyx Intellectual Property, Option Product Improvements Controlled by Ultragenyx and Joint Intellectual Property for use in the Licensed Field in the Territory solely to perform its obligations under each Research Plan and to the extent necessary or reasonably useful for Takeda to evaluate a Candidate Product.

(c) **No Implied Licenses**. No license or other right is or shall be created or granted hereunder during the Collaboration Term with respect to any Research Product by implication,

estoppel, or otherwise. All rights not expressly granted by a Party under this Agreement are reserved by such Party and may not be used by the other Party for any purpose.

6.6 **Research Materials Transfer**.

(a) In order to facilitate the activities contemplated by this Agreement, Takeda shall transfer to Ultragenyx, at no cost to Ultragenyx (i) those quantities of [***] Compound Controlled by Takeda as of the Execution Date as are necessary for Ultragenyx to perform the activities allocated to it under the [***] Research Plan and (ii) reasonable quantities of biological materials or chemical compounds Controlled by Takeda at the time a Candidate Product becomes an Option Product for Development of such Option Product (collectively, the "Research Materials") by Ultragenyx in furtherance of the applicable Research Plans. Such transfer shall be pursuant to a mutually agreed upon Research Materials transfer plan and schedule (including, as necessary, a separate agreement with respect to such transfer which the Parties shall enter as soon as practicable (A) after the Effective Date in the case of the foregoing clause (i) or (B) after a Candidate Product becomes an Option Product in the case of the foregoing clause (ii)). Except as otherwise provided for under this Agreement, all such Research Materials will remain the sole property of Takeda, will be used only in furtherance of the activities conducted in accordance with the applicable Research Plans, will not be used or delivered to or for the benefit of any Third Party (except for subcontractors in furtherance of the Research Plans), without the prior written consent of Takeda, and will be used in compliance with Applicable Law. The Research Materials supplied under this Agreement must be used with prudence and appropriate caution in any experimental work because not all of their characteristics may be known. Takeda will provide Ultragenyx the most current material safety data sheet for the Research Materials upon transfer of any Research Materials.

(b) Except as expressly set forth in this Agreement, THE RESEARCH MATERIALS ARE PROVIDED "AS IS" AND WITHOUT ANY REPRESENTATION OR WARRANTY, EXPRESS OR IMPLIED, INCLUDING ANY IMPLIED WARRANTY OF MERCHANTABILITY OR OF FITNESS FOR ANY PARTICULAR PURPOSE OR ANY WARRANTY THAT THE USE OF THE RESEARCH MATERIALS WILL NOT INFRINGE OR VIOLATE ANY PATENT OR OTHER PROPRIETARY RIGHTS OF ANY THIRD PARTY.

6.7 **General Terms Applicable to Research Plans and Research Activities**.

(a) **Annual Review of Research Plans**. On an annual basis, the Parties, through the JRC, shall review, and as necessary, update and amend the then-current Research Plans, provided that either Party may at any time between annual updates recommend updates or amendments of the then-current plans and associated budget for consideration by the JRC.

(b) **Performance Obligations**. With respect to each Research Plan, Ultragenyx and Takeda shall each use Commercially Reasonable Efforts to execute and perform the activities assigned to it and cooperate with the other Party in the performance of such activities. Each Party shall conduct the activities assigned to it under the Research Plan in a good scientific manner and in compliance in all material respects with Applicable Law, including applicable

national and international (e.g., ICH, GCP, GLP, and GMP) guidelines. If a Research Plan provides for Clinical Trials, the sponsor of such trial shall register and post the results of such trial.

(c) **Records; Disclosure of Data and Results**. Each Party shall prepare and maintain, or shall cause to be prepared and maintained, complete and accurate written records, accounts, notes, reports and data with respect to its activities conducted pursuant to a Research Plan in conformity with Applicable Law and standard pharmaceutical industry practices; provided that in no case shall such records be maintained for less than three (3) years following the Calendar Year to which such records pertain (or such longer period as may be required by Applicable Laws). Upon the other Party's written request, the Party receiving such written request shall send legible copies of the aforesaid to the other Party throughout the Term with respect to such Research Product and for a minimum of twelve (12) months following such Term. Upon reasonable advance notice, at the request of the JRC, each Party agrees to make its employees and consultants reasonably available at their respective places of employment to consult with the other Party on issues arising in connection with each Research Plan. In accordance with the reporting format and schedule approved by the JRC, each Party shall promptly disclose to the other Party in writing all data, including preclinical data, clinical trial data (if any), formulation data and Manufacturing data, generated by or on behalf of such Party with respect to a Research Product in the Licensed Field in the Territory.

(d) **Termination of Research Plan**. In the event the activities under a Research Plan are terminated for any reason, all research thereunder shall cease and the applicable Option Product or [***] Product will be deemed to be a Terminated Product. All Terminated Products shall revert to Takeda pursuant to Section 15.7(c). For clarity, such termination shall not terminate the Collaboration Term for any other purpose under this Agreement.

6.8 **Research Program Expenses.**

(a) **Nomination Evaluation**. Each Party shall be responsible for its own FTEs and any Third Party expenses, in each case, incurred with respect to the nomination, evaluation and selection of Candidate Products in accordance with Section 6.2(a).

(b) **[***] Research Plan**. Ultragenyx shall reimburse Takeda for Takeda's FTE Costs and out-of-pocket Third Party expenses, in each case, incurred by Takeda in furtherance of the completion of those activities assigned to it under the [***] Research Plan and in accordance with the applicable budget, subject to a maximum reimbursement obligation of [***] of such budget or such greater amount as Ultragenyx may approve in advance.

(c) **Validation Research Plan**. Takeda shall be responsible for its own FTEs and any Third Party expenses incurred by Takeda with respect to a Validation Research Plan.

(d) **Option Product Research Plan.** Ultragenyx shall reimburse Takeda for Takeda's FTE Costs and out-of-pocket Third Party expenses, in each case, incurred by Takeda in furtherance of the completion of those activities assigned to it under an Option Product Research Plan and in accordance with the applicable budget, subject to a maximum reimbursement

obligation of [***] of such budget or such greater amount as Ultragenyx may approve in advance.

6.9 **Invoices**. Within forty-five (45) days after the end of each Calendar Quarter, Takeda will provide a written report and invoice to Ultragenyx setting forth in reasonable detail its FTEs and its Third Party expenses recorded in furtherance the [***] Research Plan and Option Product Research Plans. Within sixty (60) days after the receipt of such invoice, Ultragenyx shall pay the undisputed portion of any such invoice. For clarity, making such a payment does not preempt Ultragenyx's audit rights under Section 11.12, which remain in full force and effect. If Ultragenyx in good faith identifies items in an invoice which are disputed, Ultragenyx will notify Takeda in writing, noting its objection to the disputed item(s) with specificity, within ten (10) business days of receipt of the invoice. Takeda will respond to such written notification within ten (10) days of receipt of the disputed notification. Thereafter, the Parties shall negotiate in good faith to resolve the dispute with either Takeda supplying Ultragenyx documentation justifying the charge or reducing or deleting the disputed amount. Any dispute over invoiced amounts due that cannot be resolved by direct good faith negotiation between the Parties shall be resolved in accordance with ARTICLE 16 (Dispute Resolution) of this Agreement; provided further, if the Dispute is not resolved pursuant to Section 16.2, the Parties agree that such Dispute shall be resolved pursuant to Section 16.3.

6.10 **Option Products.**

(a) At any time during the Collaboration Term after the completion of research activities under a Validation Research Plan, either Ultragenyx or Takeda may, through the JRC, nominate a Candidate Product for selection as an Option Product, and the JRC will promptly consider such request. In order for a Candidate Product to become an Option Product, the JRC must agree (by mutual agreement of the Parties' representatives on the JRC) to (i) the selection of the Candidate Product as an Option Product, (ii) a research plan, and budget that identifies the research and development activities which shall be performed and paid for entirely by Ultragenyx (each, an "Option Product Research Plan"), and (iii) key terms, including the territory, field of use, development and commercial responsibilities and financial terms (the "Option Product Key Terms") to serve as the basis for an Option Product License Agreement. For clarity, the Option Product Research Plan for [***] Products is the [***] Research Plan.

(b) The [***] Products are designated as Option Products as of the Effective Date. The Option Product Key Terms for [***] Products are attached hereto as Exhibit 6.10(b).

6.11 **The Ultragenyx Option.** Takeda hereby grants to Ultragenyx, during the applicable Collaboration Term, the exclusive option to obtain, on a product-by-product basis, an exclusive license, with the right to grant sublicenses through multiple tiers, under the Option Product Technology and Joint Intellectual Property to Exploit (a) the [***] Products and (b) up to five (5) other Option Products in the Licensed Field in the Territory (the "Ultragenyx Option"), subject to the terms and conditions set forth in this Agreement including ARTICLE 8.

6.12 **Exercising the Option**.

(a) At any time during the Collaboration Term, Ultragenyx may exercise the Ultragenyx Option regarding an Option Product by notifying Takeda in writing of its intent to exercise the Option with respect to a specific Option Product and negotiate the terms of a license agreement (the "Option Notice"). During the period of time beginning on the effective date of each such Option Notice and ending [***] thereafter, which period may be extended by mutual agreement (the "Option Negotiation Period"), the Parties will conduct good faith negotiations with the intent to agree upon license terms and conclude a definitive license agreement (the "Option Product License Agreement") in accordance with the applicable Option Product Key Terms and other terms that reflect the expected commercial opportunity and development stage of the Option Product. Any such Option Product License Agreement will include provisions to address approvals of any Governmental Authority which are required before effectiveness of such Option Product License Agreement.

(b) If the Parties cannot conclude an Option Product License Agreement during the Option Negotiation Period, Takeda and Ultragenyx shall each have the right to submit the Option Product Key Terms and other terms for a final decision regarding the terms of the Option Product License Agreement pursuant to binding arbitration under Section 16.3. All rights to any Option Product for which the Parties do not enter into an Option Product License Agreement shall revert to Takeda and such Option Product shall be deemed a Terminated Product subject to Section 15.7(c).

ARTICLE 7 – TAKEDA RESEARCH SUPPORT

7.1 **Research Support.** During the Collaboration Term and upon mutual agreement of the Parties, Takeda may provide research support as set forth in this Section 7.1 ("Research Support") to Ultragenyx, at Ultragenyx's sole cost. Such Research Support shall be related to the development of Ultragenyx Pipeline Products (in each case, other than Exercised Products) or Licensed Option Products (in each case, in connection with an Option Product License Agreement), and shall include medicinal chemistry, testing of compounds in disease animal models, drug formulation and clinical development support. If Ultragenyx and Takeda agree that Takeda should provide such Research Support, the confidentiality obligations, access to premises, and other details related to Takeda personnel providing such Research Support to Ultragenyx shall be addressed in a separate agreement between the Parties and such personnel.

7.2 **Expenses and Invoices.** Ultragenyx shall reimburse Takeda for Takeda's FTE Costs and out-of-pocket Third Party expenses, in each case, incurred by Takeda for the provision of the Research Support and in accordance with the applicable budget, subject to a maximum reimbursement obligation of [***] of such budget or such greater amount as Ultragenyx may approve in advance. Within forty-five (45) days after the end of each Calendar Quarter, Takeda will provide a written report and invoice to Ultragenyx setting forth in reasonable detail its FTEs and its Third Party expenses recorded for the Research Support. Within sixty (60) days after the receipt of such invoice, Ultragenyx shall pay the undisputed portion of any such invoice. For clarity, making such a payment does not preempt Ultragenyx's audit rights under Section 11.12, which remain in full force and effect. If Ultragenyx in good faith identifies items in an invoice which are disputed, Ultragenyx will notify Takeda in writing,

noting its objection to the disputed item(s) with specificity, within ten (10) business days of receipt of the invoice. Takeda will respond to such written notification within ten (10) days of receipt of the disputed notification. Thereafter, the Parties shall negotiate in good faith to resolve the dispute with either Takeda supplying Ultragenyx documentation justifying the charge or reducing or deleting the disputed amount. Any dispute over invoiced amounts due that cannot be resolved by direct good faith negotiation between the Parties shall be resolved in accordance with ARTICLE 16 (Dispute Resolution) of this Agreement; provided further, if the Dispute is not resolved pursuant to Section 16.2, the Parties agree that such dispute shall be resolved pursuant to Section 16.3.

7.3 **Patent Ownership.** If Research Support is provided pursuant to Section 7.1 related to an Ultragenyx Pipeline Product (other than an Exercised Product), then, notwithstanding Section
12.1 or any other separate written agreement between the Parties with respect to such Research Support, as between the Parties and regardless of inventorship, Ultragenyx shall own all right, title and interest in and to any Patents related to such Ultragenyx Pipeline Product (other than an Exercised Product in the Exercised Countries) that arise out of such Research Support. For purposes of clarity, following the execution of an Option Product License Agreement or Exercised Product License Agreement, the terms of such license agreement shall govern the handling of activities of the type covered by the definition of Research Support related to the Product(s) that are the subject of the applicable license agreement.

ARTICLE 8 – TAKEDA'S LICENSE OPTION

8.1 **The License Option.** In partial consideration for the premium paid by Takeda to Ultragenyx under the Common Stock Purchase Agreement, Ultragenyx hereby grants to Takeda during the applicable Takeda Option Term, the exclusive option to obtain (the "Takeda Option"), on a product-by-product and country-by-country basis, an exclusive license (even as to Ultragenyx and its Affiliates) to (a) any or all of the Licensed Products in the Ultragenyx Field,
(b) any or all Licensed Option Products in the Licensed Field, and (c) one (1) Ultragenyx Pipeline Product in the Licensed Field, in each case in any or all of the countries in the Takeda Territory. For clarity, if Takeda elects not to exercise the Takeda Option with respect to (i) any Licensed [***] Product, Licensed Analog Product, Licensed Option Product, or Ultragenyx Pipeline Product, or (ii) any country in the Takeda Territory, as the case may be, prior to the expiration of the Takeda Option Term with respect to such Product and/or such country, as applicable, then Takeda shall no longer have any rights under the Takeda Option with respect to such Product and/or such country, as applicable.

8.2 **Exercising the License Option**.

(a) **Preparation and Delivery of the Data Packages**. Ultragenyx shall prepare and deliver to Takeda as soon as reasonably practicable after completion of the applicable Clinical Trials (a) the Final Phase II Data Package for each Licensed [***] Product, Licensed Analog Product, Licensed Option Product and Ultragenyx Pipeline Product (other than [***]) and (b) the Final Phase III Data Package for [***].

(b) **Takeda Review of Research Data Package**. Following Takeda's receipt of the applicable Data Package pursuant to Section 8.2(a) and during the applicable Takeda Option Term, Takeda may review and assess the Data Package to determine whether it will submit the Takeda Option Notice. During this review period, upon Takeda's reasonable request, Ultragenyx shall promptly make available to Takeda: (i) its employees, consultants and independent contractors (subject to the availability of any independent contractors) who performed the activities on behalf of Ultragenyx, including the preparation of the Data Package; and (ii) any additional Information under Ultragenyx's possession and Control related to the applicable products that is reasonably useful in evaluating the Data Package.

(c) **Takeda Option Exercise Mechanics**. Takeda may exercise the Takeda Option for one or more Licensed [***] Products, one or more Licensed Analog Products, one or more Licensed Option Products, and one Ultragenyx Pipeline Product on a country-by-country basis in the Takeda Territory at any time during the applicable Takeda Option Term by providing written notice to Ultragenyx (the "Takeda Option Notice") identifying the applicable Products ("Exercised Products") and countries ("Exercised Countries"); provided, however, that Takeda may exercise the Takeda Option with respect to each Licensed Product only once (i.e., if the Takeda Option is exercised with respect to a particular Licensed Product for fewer than all applicable countries, then additional countries may not be added by additional exercises of the Takeda Option with respect to that particular Licensed Product).

(d) During the period of time beginning on the effective date of the Takeda Option Notice and ending [***], which period may be extended by mutual agreement (the "Takeda Option Negotiation Period"), the Parties will conduct good faith negotiations to conclude a definitive license agreement (the "Exercised Product License Agreement"). Such Exercised Product License Agreement shall include the following:

(i) the following license grant with respect to the Exercised Products in the Exercised Countries, which, to the extent of any conflict, shall supersede the Ultragenyx [***] License and Takeda [***] License and the terms of any Option Product License Agreement: Ultragenyx hereby grants to Takeda an exclusive license (even as to Ultragenyx and its Affiliates), with the right to grant sublicenses through multiple tiers, under the Ultragenyx Intellectual Property and Joint Intellectual Property, to Exploit the Exercised Products in the Ultragenyx Field (where such Exercised Product is a Licensed Product) or the Licensed Field (where such Exercised Product is a Licensed Option Product or Ultragenyx Pipeline Product) in the Exercised Countries;

(ii) financial terms in ARTICLE 11 (and related definitions) applicable to Exercised Products (and no other consideration payable by Takeda);

(iii) provisions to address approvals of any Governmental Authority which are required before effectiveness of the Exercised Product License Agreement;

(iv) provisions to address the prosecution, enforcement and defense of Patents that cover Exercised Products similar to those contained in ARTICLE 12;

written notice;

(v) the right for Takeda to terminate for convenience upon [***]

(vi) the right for Takeda to, in lieu of termination for Ultragenyx's material breach or insolvency, receive rights on the basis set forth in Section 15.7(a)(ii)(B);

(vii) provisions that upon the expiration of the Takeda Royalty Term for each Exercised Product in each Exercised Country, Takeda shall have a non-exclusive, fully-paid up and irrevocable license under the Ultragenyx Intellectual Property with respect to such Exercised Product in such Exercised Country in the Ultragenyx Field (for Exercised Products that are Licensed Products) and in the Licensed Field (for Exercised Products that are Option Products or Ultragenyx Products); and

(viii) to the extent applicable, Miscellaneous provisions as contained in ARTICLE 18.

(e) If the Parties cannot conclude the Exercised Product License Agreement during the Takeda Option Negotiation Period, Takeda and Ultragenyx shall each have the right to submit the terms for a final decision regarding the terms (other than those specified in Section 8.2(d)) of the Exercised Product License Agreement pursuant to binding arbitration under Section 16.3. For clarity, the terms set forth in Section 8.2(d) must be included within the Exercised Product License Agreement and are not subject to arbitration and Ultragenyx shall be required to enter into an Exercised Product License Agreement including those terms if the Takeda Option is exercised pursuant to Section 8.2(c).

8.3 **Takeda Right of First Negotiation on Ultragenyx Pipeline Products.** As additional consideration for the premium being paid by Takeda to Ultragenyx under the Common Stock Purchase Agreement, and notwithstanding anything to the contrary contained in this Agreement, if, during [***] following expiration of the applicable Takeda Option Term, Ultragenyx intends to license (all or a subset of all rights) or otherwise transfer any Ultragenyx Pipeline Product to a Third Party in the Takeda ROFN Territory, Ultragenyx will provide Takeda with prior written notice of such intent and, for a period of [***] after receipt of such notice, Takeda will have a right of first negotiation to enter into a definitive agreement with Ultragenyx for such license (of all or a subset of all rights) or other transfer in the Takeda ROFN Territory. If the Parties fail to enter into a definitive agreement prior to the expiration of [***], Ultragenyx will have the right to enter into a definitive agreement with a Third Party for the license (of all or a subset of all rights) or other transfer of such Ultragenyx Pipeline Product in the Takeda ROFN Territory.

8.4 **Transition of Responsibilities After Exercise of the Takeda Option**. Ultragenyx shall, in accordance with a transition plan set forth in the Exercised Product License Agreement, transfer to Takeda all activities and responsibilities related to the Exercised Products in the Exercised Countries. The Parties shall exercise Commercially Reasonable Efforts to complete the transfer in accordance with such transition plan. Any dispute between the Parties regarding the transition shall be resolved as set forth in the Exercised Product License Agreement.

8.5 **Development and Commercialization After Exercise of the Takeda Option**. After exercise of the Takeda Option, Takeda will use Commercially Reasonable Efforts to Exploit the Exercised Products in the Takeda Option Field in the Exercised Countries at its sole cost and expense; provided, however, notwithstanding the above, Takeda's financial commitment toward global Development costs for Licensed Option Products and an Ultragenyx Pipeline Products will be in accordance with the terms set forth in Section 8.6.

8.6 **Cost Sharing for Development Activities in Takeda Territory**. After exercise of the Takeda Option with respect to a Licensed Option Product and/or an Ultragenyx Pipeline Product:

(a) the Parties will share the costs of future global Development activities for such Licensed Option Product or Ultragenyx Pipeline Product, as applicable, including costs for Clinical Trials and clinical drug supply and chemistry, manufacturing and controls-related activities in accordance with mutually agreed upon Development plans, budgets and cost sharing structures; provided that Takeda shall only be required to share global Development costs where the Development activities are necessary or reasonably useful to support the Development, Regulatory Approval and Commercialization of such product in the Takeda Territory, in which case Takeda will contribute [***]. For clarity, Takeda will not be required to share in the costs of future global Development activities where the Development activities, including Clinical Trials, are not necessary and are not used to support the Development,
Regulatory Approval and Commercialization of such product in the Takeda Territory; and

(b) Notwithstanding the foregoing, Takeda shall be solely responsible for all Development costs where the Development activities are required specifically and solely for Regulatory Approval of a Licensed Option Product or Ultragenyx Pipeline Product, as applicable, in the Takeda Territory. If such Development activities are also necessary or reasonably useful for Regulatory Approval of a Licensed Product, Licensed Option Product or Ultragenyx Pipeline Product, as applicable, outside the Takeda Territory, the Parties will negotiate in good faith to agree upon an equitable sharing of costs for such Development activities.

ARTICLE 9 – REGULATORY

9.1 **Lead Regulatory Party**. Primary regulatory responsibility under this Agreement shall be assigned to one of the Parties (such Party, the "Lead Regulatory Party") as set forth in this Section 9.1.

(a) Ultragenyx shall be the Lead Regulatory Party for all Licensed Products until expiration of the [***] Option Term. Following expiration of the [***] Option Term, whether or not Ultragenyx has exercised the [***] Option (i) Takeda shall be the Lead Regulatory Party for Licensed [***] Products in the Takeda Field unless otherwise agreed by the Parties, and (ii) Ultragenyx shall be the Lead Regulatory Party for Licensed [***] Products in the Ultragenyx Field and shall be the Lead Regulatory Party for Licensed Analog Products in the Ultragenyx Field.

(b) Ultragenyx shall be the Lead Regulatory Party for all Ultragenyx Pipeline Products in the Territory until expiration of the Takeda Option Term. Following the expiration of the Takeda Option Term, Ultragenyx shall be the Lead Regulatory Party in the Territory for all Ultragenyx Pipeline Products for which the Parties have not entered into an Exercised Product License Agreement. For clarity, at all times Ultragenyx shall be the Lead Regulatory Party for all Ultragenyx Pipeline Products outside of the Takeda Territory. If Takeda exercises the Takeda Option with respect to an Exercised Product, the Exercised Product License Agreement shall provide that Takeda shall be the Lead Regulatory Party for such Exercised Product in the Licensed Field in the Takeda Territory.

(c) The Parties will agree as to which Party shall be the Lead Regulatory Party for the [***] Products and each Candidate Product prior to the expiration of the Collaboration Term; provided, however, that Takeda shall be the Lead Regulatory Party (i) if the Parties are unable to agree, (ii) at any time after Ultragenyx provides Takeda written notice that it will not exercise the Ultragenyx Option with respect to the [***] Products and (iii) for the planned Scientific Advice with the Dutch Medicines Evaluation Board and US Orphan Drug Designation follow-up (as needed) for [***]. Ultragenyx shall be the Lead Regulatory Party for each Option Product for which the Parties have entered into an Option Product License Agreement and Takeda shall be the Lead Regulatory Party for each Option Product for which the Parties have not entered into an Option Product License Agreement.

(d) In accordance with the foregoing, upon entering into an Option Product License Agreement or Exercised Product License Agreement, it is understood that the terms of such Option Product License Agreement or Exercised Product License Agreement will govern with respect to such Option Product covered by such Option Product License Agreement or Exercised Product covered by such Exercised Product License Agreement, as applicable.

9.2 **Initial Transfer of Data and Regulatory Materials**.

(a) **Transfer to Ultragenyx**

(i) As soon as practicable after the Effective Date, but in any event no later than sixty (60) days after the Effective Date, Takeda shall timely transfer to Ultragenyx copies of (A) all Regulatory Materials (in electronic or other format) in its possession related to the use of the Licensed [***] Products in the Ultragenyx Field (and, solely for purposes of Ultragenyx's performance of its obligations under Section 4.3(a)(ii), in the Takeda Field) and (B) the briefing book, FDA meeting minutes, Takeda meeting minutes, and FDA correspondence associated with [***], the US Orphan Drug Designation Request and subsequent regulatory correspondence, and the briefing book and correspondence for Scientific Advice with the Dutch Medicines Evaluation Board, in each case for the [***] Products in the Licensed Field and existing as of such date of transfer. Following each such transfer and at a time to be mutually agreed by the Parties, the Parties shall take all steps necessary (a) for Ultragenyx to own or have the right of reference to the INDs and Regulatory Approvals necessary to conduct Development of the Licensed [***] Product in the Ultragenyx Field and (b) for Takeda to own or have the right of reference to the INDs and Regulatory Approvals necessary to conduct Development of the Licensed [***] Product in the Takeda Field.

(ii) Within sixty (60) days after the Effective Date, Takeda shall make available to Ultragenyx separate copies (in electronic or other format) of the study reports from all non-clinical trials and Clinical Trials in the Territory, in each case, whether completed as of the Effective Date or then in-progress, that are Controlled by Takeda (to the extent not previously provided to Ultragenyx), as such reports become available to Takeda, and to the extent that they relate to the use of the Licensed [***] Products for the Territory.

(b) **Transfer to Takeda**

(i) As soon as practicable after the effective date of an Exercised Product License Agreement for a given Exercised Product, but in any event no later than sixty (60) days after such date, Ultragenyx shall timely transfer to Takeda copies of all Regulatory Materials (in electronic or other format) in its possession related to the use of the Exercised Product in the Exercised Countries and which support the Product INDs, the Product Regulatory Approvals and associated correspondence, existing as of such date of transfer. Promptly after such transfer, Ultragenyx shall take all steps necessary to transfer ownership of all such Product INDs and Product Regulatory Approvals in the Takeda Territory to Takeda, including, if applicable, submitting to the PMDA a letter or other necessary documentation (with a copy to Takeda) notifying the PMDA of the transfer of such ownership. From time to time after the IND Date, and solely to the extent not previously disclosed, Ultragenyx shall, and shall cause its Affiliates to, without additional compensation, disclose and make available to Takeda, in whatever form Takeda may reasonably request, all Regulatory Materials Controlled by Ultragenyx and related to the use of an Exercised Product in the Exercised Countries.

(ii) Within sixty (60) days after the Parties enter into an Exercised Product License Agreement for a given Exercised Product, Ultragenyx shall make available to Takeda separate copies (in electronic or other format) of the study reports from all non-clinical trials and Clinical Trials in the Territory, in each case, whether completed as of the Effective Date, that are Controlled by Ultragenyx (to the extent not previously provided to Takeda), as such reports become available to Ultragenyx, and to the extent that they relate to the use of the Exercised Products in the Exercised Countries.

9.3 **Preparation of Regulatory Materials**.

(a) After the Effective Date (or, as applicable, the IND Date), the Lead Regulatory Party shall have the sole right and responsibility, and shall exercise Commercially Reasonable Efforts, to prepare, obtain, and maintain, as applicable, the Regulatory Materials, including the Product INDs, the Product Regulatory Approvals, and other submissions, and to conduct communications with the FDA, for the relevant Products in the applicable indication in the Territory or applicable portion thereof, except in the case of Licensed [***] Products from the Effective Date until expiration of the [***] Option Term, during which time Takeda shall hold the IND and Ultragenyx (i.e., the Lead Regulatory Party) shall receive a right of reference from Takeda. Except with respect to Licensed [***] Products from the Effective Date until expiration of the [***] Option Term, all Product INDs and Product Regulatory Approvals generated after the Effective Date, including any supplements or amendments to those Product INDs and Product Regulatory Approvals in existence as of the Effective Date, with respect to such Products in the

applicable indication in the Territory or applicable portion thereof under this Agreement shall be owned by, and shall be the sole property and held in the name of, Lead Regulatory Party or its designee.

(b) Other than the Scientific Advice Briefing Book for the [***] Products which has been prepared as of the Execution Date but not yet been submitted, the Lead Regulatory Party shall provide the other Party with an opportunity to review and comment on all material Regulatory Materials submitted by the Lead Regulatory Party to a Regulatory Authority after the Effective Date, in each case reasonably in advance of when the Lead Regulatory Party intends to submit such Regulatory Materials to the applicable Regulatory Authority. The other Party shall provide its comments within [***], or such other period of time mutually agreed to by the Parties. The Lead Regulatory Party shall consider in good faith any such comments of the other Party. The Lead Regulatory Party shall provide the other Party with a copy in electronic form of all material Regulatory Materials filed with the Regulatory Authority related to the use of the relevant Products.

(c) The Lead Regulatory Party shall notify the other Party within no less than [***] of any request for a meeting or substantive telephone conference call with a Regulatory Authority with respect to any Product IND or Product Regulatory Approval. Upon the other Party's request, the Lead Regulatory Party shall request that the FDA or other Regulatory Authority permit at least [***] of the other Party's employees to attend any such meeting or conference call. To the extent permitted by the FDA or other Regulatory Authority, the other Party shall have the right to participate in any such meeting or conference call. The foregoing rights and obligations apply with respect to meetings or conferences initiated by the Lead Regulatory Party or by a Regulatory Authority. The Lead Regulatory Party shall promptly furnish the other Party with copies of all substantive correspondence related to the relevant Product the Lead Regulatory Party has had with the Regulatory Authority, and contact reports concerning substantive conversations or minutes from any substantive meetings with a Regulatory Authority related to such Product.

(d) Notwithstanding the foregoing, Takeda, in consultation with Ultragenyx, shall be responsible for the preparation of any components of Regulatory Materials to be filed by Ultragenyx that relate to the Manufacture of a Licensed Product or Option Product. Takeda shall use Commercially Reasonable Efforts to prepare such components in a timely manner and provide such components to Ultragenyx with sufficient time for Ultragenyx to review and comment on such components; provided, however, that Takeda may use an alternative arrangement (such as a drug master file) to preserve the confidentiality of such components to the extent required by any Third Party agreements or, in Takeda's reasonable discretion, if otherwise necessary to protect Takeda confidential information and such alternative arrangement is permissible under Applicable Laws; provided, further, that if Ultragenyx reasonably requests additional information with respect to the Development or Commercialization of a Licensed Product or Option Product otherwise treated as confidential in such alternative arrangement (such as a drug master file), Takeda shall reasonably consider such request. In the event that Ultragenyx elects to Manufacture a Licensed Product or Option Product, Ultragenyx shall notify Takeda of such election and, to the extent covered by the license rights granted in Sections 3.1(a)

and 3.1(c) (for Licensed Products) or Section 6.5(a) (for Option Products), Takeda shall promptly transfer to Ultragenyx or its Third Party designee all Regulatory Materials, processes and technical information Controlled by Takeda or its Affiliates that are reasonably necessary and useful for the Manufacture of such Licensed Product or Option Product, and thereafter Ultragenyx shall be responsible for the preparation of any components of Regulatory Materials to be filed related to the Manufacture by Ultragenyx or its Third Party designee of such Licensed Product or Option Product.

9.4 **Cooperation, Consultation and Review**.

(a) The Parties shall cooperate with each other to achieve the regulatory objectives contemplated herein in a timely, accurate and responsive manner and shall assist the other Party as reasonably requested in connection with the preparation and filing of Regulatory Materials in the Licensed Field, whether in or outside of the Territory. The Parties shall establish a joint regulatory working group to manage Licensed Product regulatory activities and issues. It is the intention of the Parties that the joint regulatory working group shall meet (in person or via teleconference) on an as-needed basis after the Effective Date and throughout the Term, but at a minimum on a quarterly basis. The Parties agree and acknowledge that the activities of Ultragenyx with respect to (i) Licensed [***] Products in the Ultragenyx Field and (ii) Licensed Analog Products in the Licensed Field and the activities of Takeda with respect to (A) Licensed [***] Products in the Takeda Field and (B) Licensed Products outside of the Licensed Field, shall be coordinated such that they are consistent with the overall objective of facilitating Regulatory Approvals.

(b) The other Party shall assist the Lead Regulatory Party, as is reasonably necessary, in order for the Lead Regulatory Party to obtain and maintain the Product INDs and the Product Regulatory Approvals, including in connection with the preparation and filing of Regulatory Materials necessary to maintain such Product INDs and Product Regulatory Approvals.

9.5 **Regulatory Costs and Expenses**. Each Party shall bear its own costs and expenses incurred related to the preparation, maintenance, formatting and filing of the Regulatory Materials.

9.6 **Rights of Reference to Regulatory Materials**. Each Party hereby grants to the other Party a right of reference to all Regulatory Materials, including any data relied on in support of such Regulatory Materials, solely for the purpose of seeking, obtaining and maintaining Regulatory Approvals for the Products, consistent with the roles of the Parties set forth in this Agreement.

9.7 **Labeling Information Exchange/Labeling Agreement**. The Parties shall cooperate to develop methods and/or procedures for sharing information related to Labeling. Specific details regarding the management of Labeling information, including CCDS will be delineated in a separate Labeling agreement that shall be agreed upon by the Parties.

9.8 **Adverse Event Reporting and Safety Data Exchange**.

(a) **Safety Information Exchange; Pharmacovigilance Agreement**.

(i) The Parties shall cooperate to develop methods and/or procedures for sharing information relating to the clinical experiences in accordance with safety reporting requirements of the respective Regulatory Authorities and as necessary for a Party to comply with Applicable Laws. Specific details regarding the management of safety information including adverse events reports related to the Development and the Commercialization of the Products will be delineated in a separate global pharmacovigilance agreement (the "PVA") that shall be agreed to by the Parties as soon as reasonably practicable, but in any event not later than [***] of the Effective Date. The Lead Regulatory Party shall be responsible for the compliance and filing of all required safety reports to the Regulatory Authorities in the Territory, including annual safety reports, throughout the Term.

(ii) The PVA shall provide as follows:

(A) Unless otherwise agreed by the Parties, the Lead Regulatory Party shall maintain the global safety database for the Products, and mirror databases will be maintained by the other Party; provided, however, that Takeda shall maintain the global safety database regarding Licensed [***] Products, and Ultragenyx shall maintain the global safety database regarding Licensed Analog Products. For clarity, to the extent a Party is no longer actively Developing or Commercializing a Licensed [***] Product, then the global safety database shall be transferred to the Party that continues to actively Develop or Commercialize such Licensed [***] Product.

(B) Each Party shall timely report to the other Party all clinical experiences, safety monitoring, and pharmacovigilance surveillance observed in the Territory, which in all cases shall be (i) for clinical studies: as soon as practicable, [***] and (ii) for commercial Products: [***]; exchange of information shall be on a Council for International Organizations of Medical Sciences Suspect Adverse Reaction Report Form ("CIOMS Form").

(C) The other Party shall prepare and provide to the Lead Regulatory Party on a timely basis safety updates in order for the Lead Regulatory Party to meet the safety report submission requirements necessary to maintain the Product INDs and the Product Regulatory Approvals.

(b) **Regulatory Reporting of Safety Information**. The Parties shall work together to achieve consensus with respect to safety issues related to the Products, including urgent safety information, and to report said opinion to safety boards, investigators, and to applicable Regulatory Authorities. In the event that, after reasonable medical and scientific consultation, the Parties cannot achieve consensus with respect to safety issues to be reported to any applicable Regulatory Authority, the Lead Regulatory Party shall have final decision making

authority with respect to the Products in the Licensed Field in the Territory. Notwithstanding anything to the contrary in this Agreement, either Party may report safety matters to a Regulatory Authority that it reasonably determines are necessary to report prior to the conclusion of the dispute resolution procedure.

9.9 **Regulatory Authority Communications Received by a Party**. Each Party shall inform the other Party in a timely manner, not to exceed [***], of the notification of any action by, or notification or other information which it receives (directly or indirectly) from any Regulatory Authority which: (i) raises any material concerns regarding the safety or efficacy of a Product; (ii) indicates or suggests a potential material liability of either Party to Third Parties in connection with a Product; (iii) is reasonably likely to lead to a recall or market withdrawal of a Product; or (iv) relates to expedited reports of adverse events with respect to a Product, or Product Complaints, and which may have a material impact on obtaining or maintaining Regulatory Approval or the continued Commercialization of a Product, as then conducted. The other Party will fully cooperate with and assist such Party in complying with regulatory obligations and communications, including by providing to such Party, in a timely manner after a request, such information and documentation in the other Party's possession as may be necessary or helpful for the Party to prepare a response to an inquiry from a Regulatory Authority. Each Party will provide the other Party in a timely manner with a copy of all correspondence received from a Regulatory Authority specifically regarding the matters referred to above.

9.10 **Audit**. If a Regulatory Authority desires to conduct an inspection or audit of a Party's facility or a facility under contract with such Party with regard to a Product in the Territory, then the audited Party shall notify the other Party as soon as practicably possible after receipt of such notification of such audit or inspection and provide copies of any materials provided to it by the applicable Regulatory Authority; provided, that the audited Party shall not be required to notify the other Party of audits or inspections that are of a routine nature or that do not relate to a Product, except where such audits result in communications or actions of such Regulatory Authority which have a direct impact upon a Product. In addition, if a Regulatory Authority conducts an unannounced inspection or audit of a Party's facility or a facility under contract with such Party with regard to a Product in the Territory, then the audited Party shall notify the other Party within [***] of commencement of such audit or inspection. The audited Party shall cooperate, and shall use reasonable efforts to cause the contract facility to cooperate, with such Regulatory Authority and the other Party during such inspection or audit. Following receipt of the inspection or audit observations of such Regulatory Authority (a copy of which the audited Party will immediately provide to the other Party), the audited Party will also provide the other Party with copies of any written communications received from Regulatory Authorities with respect to such facilities in a timely manner after receipt, to the extent such written communications relate directly to a Product or the Manufacture thereof, and will prepare the response to any such observations. The audited Party will provide the other Party with a copy of any proposed response to such communications and will consider in good faith such other Party's reasonable comments with respect to such proposed response. The audited Party agrees to conform its activities under this Agreement to any commitments made in such a response.

9.11 **Recalls and Voluntary Withdrawals**. Each Party shall notify the other Party promptly but in no event later than [***] following its determination that any event, incident, or circumstance has occurred that may result in the need for a recall, market suspension, or market withdrawal of a Product under any MAA or Regulatory Approval for the Product held by such Party and filed with Regulatory Authorities in the Territory, and shall include in such notice the reasoning behind such determination, and any supporting facts. Such Party shall have the sole right to make the final determination whether to voluntarily implement any such recall, market suspension, or market withdrawal in the Territory; provided that prior to any implementation of such a recall, market suspension, or market withdrawal, the such Party shall, to the extent practical, consult with the other Party and shall consider the other Party's comments in good faith. For all recalls, market suspensions or market withdrawals undertaken pursuant to this Section 9.11, such Party shall be solely responsible for the execution thereof, and the other Party shall reasonably cooperate in all such recall efforts. Subject to ARTICLE 17, such Party shall be responsible for all costs of any such recall, market suspension, or market withdrawal; provided that, the other Party shall be responsible for the costs of any recall, market suspension, or market withdrawal with respect to a Product in the Territory to the extent such recall, market suspension, or market withdrawal is attributable to the other Party's breach of its obligations hereunder or its negligence, recklessness or willful misconduct.

ARTICLE 10 – MANUFACTURING AND SUPPLY

10.1 **Supply Agreement**. The Parties shall enter into mutually agreeable supply agreements as soon as appropriate after the Effective Date covering the manufacture and research supply (other than as provided in Section 6.6), clinical supply or Commercial supply of Compounds or Products needed for Development or Commercialization.

ARTICLE 11 – PAYMENT

11.1 **Licensed Product Development Milestones Payable to Takeda**.

(a) Ultragenyx shall pay to Takeda a milestone payment within forty-five (45) days after the first achievement of each of the following milestones for each Licensed Product, calculated as follows:

(i) [***];

(ii) [***];

(iii) [***]

(iv) [***];

(v) [***]; and

(vi) [***]

(b) Each milestone payment in this Section 11.1 shall be payable only upon the first achievement of such milestone for each Licensed Product and no amounts shall be due for subsequent or repeated achievements of such milestone for the same Licensed Product.

11.2 **Licensed Product Sales Milestones Payable to Takeda**.

(a) Ultragenyx shall pay to Takeda a milestone payment within [***] after the first achievement of each of the following milestones for the aggregated annual Net Sales of all Licensed Products, calculated as follows:

(i) upon the Net Sales in the Territory of all Licensed Products made by Ultragenyx, its Affiliates and Sublicensees in a given Calendar Year equaling or exceeding [***];

(ii) upon the Net Sales in the Territory of all Licensed Products made by Ultragenyx, its Affiliates and Sublicensees in a given Calendar Year equaling or exceeding [***]; and

(iii) upon the Net Sales in the Territory of all Licensed Products made by Ultragenyx, its Affiliates and Sublicensees in a given Calendar Year equaling or exceeding [***].

(b) Each milestone payment in this Section 11.2 shall be payable only upon the first achievement of such milestone for all Licensed Products in aggregate and no amounts shall be due for subsequent or repeated achievements of such milestone. If two or more milestone events are achieved in the same Calendar Year, Ultragenyx shall pay to Takeda each milestone payment corresponding to the respective milestone event.

11.3 **Licensed Product Royalties Payable to Takeda.** Subject to Section 11.8 below, and during the applicable Licensed Product Royalty Term, Ultragenyx shall pay to Takeda, on a Licensed Product-by-Licensed Product basis, a running royalty at the following incremental royalty rates, on Net Sales of each Licensed Product in the Territory in a Calendar Year:

Net Sales in the Territory	**Royalty Rate**
For that portion of annual Net Sales less than $[***]	[***]%
For that portion of annual Net Sales greater than or	[***]%

equal to $[***] but less than $[***]	
For that portion of annual Net Sales greater than or equal to $[***] but less than $[***]	[***]%
For that portion of annual Net Sales greater than or equal to $[***]	[***]%

11.4 **Exercised Product Milestones and Fees Payable to Ultragenyx**.

(a) Pursuant to the applicable Exercised Product License Agreement, Takeda shall pay to Ultragenyx a milestone payment of [***] within [***] after the first Regulatory Approval in the first indication in Japan for [***] if such product is an Exercised Product that has not been terminated at the time of such Regulatory Approval. The milestone payment in this Section 11.4(a) shall be payable only upon the first achievement of such milestone for each such Exercised Product and no amounts shall be due for subsequent or repeated achievements of such milestone for such Exercised Product. For clarity, the maximum aggregate amount payable by Takeda for each Exercised Product pursuant to this Section 11.4(a) is [***].

(b) For all Ultragenyx Pipeline Products other than [***], during the Takeda Option Negotiation Period for such Ultragenyx Pipeline Products, the Parties will negotiate in good faith (for inclusion in the applicable Exercised Product License Agreement) commercially reasonable financial terms in addition to the royalties contemplated in Section 11.6 (such as one or more of the following: option exercise fees, sales and development milestones, reimbursement for historical research and development costs allocable to Japan, and milestones due to Third Party licensors) for such Ultragenyx Pipeline Products, taking into consideration factors such as the investment in the collaboration under this agreement already made by Takeda, including the premium paid by Takeda to Ultragenyx under the Common Stock Purchase Agreement. If the Parties cannot reach agreement on such commercially reasonable financial terms during the Takeda Option Negotiation Period, either Takeda or Ultragenyx may seek a final decision regarding the commercially reasonable financial terms pursuant to binding arbitration as set forth in Section 16.3.

11.5 **Licensed Product Royalties Payable to Ultragenyx for the Exercised Countries**. Subject to Section 11.8 below, and during the applicable Licensed Product Royalty Term, pursuant to the applicable Exercised Product License Agreement, Takeda shall pay to Ultragenyx, on a Licensed Product-by-Licensed Product basis, a running royalty at the following incremental royalty rates, on aggregate, Net Sales of each Exercised Product that is a Licensed Product in the Exercised Countries in a Calendar Year:

(a) If the Takeda Option for such Licensed Product is exercised by Takeda prior to Takeda's receipt of the Final Phase II Data Package for such Licensed Product:

Net Sales in the Exercised Countries	Royalty Rate
For that portion of annual Net Sales less than $[***]	[***]%
For that portion of annual Net Sales greater than or equal to $[***] but less than $[***]	[***]%
For that portion of annual Net Sales greater than or equal to $[***] but less than $[***]	[***]%
For that portion of annual Net Sales greater than or equal to $[***]	[***]%

(b) If the Takeda Option for such Licensed Product is exercised by Takeda after Takeda's receipt of the Final Phase II Data Package for such Licensed Product:

Net Sales in the Exercised Countries	Royalty Rate
For that portion of annual Net Sales less than $[***]	[***]%
For that portion of annual Net Sales greater than or equal to $[***] but less than $[***]	[***]%
For that portion of annual Net Sales greater than or equal to $[***] but less than $[***]	[***]%
For that portion of annual Net Sales greater than or equal to $[***]	[***]%

11.6 **Licensed Option Product and Ultragenyx Pipeline Product Royalties Payable to Ultragenyx for the Exercised Countries**. During the Takeda Option Negotiation Period for a Licensed Option Product or Ultragenyx Pipeline Product, the Parties will negotiate in good faith (for inclusion in the applicable Exercised Product License Agreement) tiered royalty rates on annual Net Sales of such Licensed Option Product or Ultragenyx Pipeline Product to be paid by Takeda to Ultragenyx during the Takeda Royalty Term. If the Parties cannot reach agreement on such tiered royalty rates during the Takeda Option Negotiation Period, either Takeda or Ultragenyx may seek a final decision regarding the royalty rates pursuant to binding arbitration as set forth in Section 16.3.

11.7 **Royalty Reduction for Generic Product Entry in a Country**. On a Licensed Product- by-Licensed Product basis, the royalty rates set forth in Sections 11.3 and 11.5 for Net Sales of a Product in a country shall be reduced by [***] in each Calendar Quarter during which the Generic Competition Percentage with respect to such Licensed Product in such country in such Calendar Quarter is greater than or equal to [***].

11.8 **Payment for Third Party Licenses**.

(a) Each Party will be responsible for paying all Third Party license fees, royalties, and/or milestones, with respect to Third Party licenses entered into by such Party or its Affiliates prior to or on the Effective Date or during the Term, for intellectual property that is necessary or reasonably useful for the Exploitation of any Licensed Product. For such Third Party licenses to Preexisting Third Party IP, the paying Party will be entitled to deduct up to [***] of such amounts due to any such Third Party from royalties payable to the other Party hereunder on such Licensed Product. For such Third Party licenses obtained during the Term, the paying Party will be entitled to deduct [***] of such amounts due to any such Third Party from royalties payable to the other Party hereunder on such Licensed Product. Notwithstanding the foregoing, in no event shall such royalty payable to Takeda in any Calendar Quarter as a result of this reduction be less than [***] of the amount that would otherwise be due.

(b) Ultragenyx shall be responsible for paying all Third Party license fees, royalties, and/or milestones, with respect to Third Party licenses for intellectual property that is necessary or reasonably useful for the Exploitation of any Ultragenyx Pipeline Product, where such licenses are entered into (i) prior to or on the Effective Date or (ii) unless and until such Ultragenyx Pipeline Product is an Exercised Product, during the Term. Each Party will be responsible for paying all Third Party license fees, royalties, and/or milestones, with respect to Third Party licenses for intellectual property that is necessary or reasonably useful for the Exploitation of any Ultragenyx Pipeline Product that is an Exercised Product entered into by such Party or its Affiliates on or after the date on which it becomes an Exercised Product. For such Third Party licenses obtained by Takeda or its Affiliates, Takeda will be entitled to deduct [***] of such amounts due to any such Third Party from royalties payable to Ultragenyx on such Exercised Product. Notwithstanding the foregoing, in no event shall the royalty payable to Ultragenyx in any Calendar Quarter on such Exercised Product as a result of this reduction be less than [***] of the amount that would otherwise be due.

(c) Notwithstanding the foregoing, for intellectual property held by a Third Party that is necessary or reasonably useful for the Exploitation of any Exercised Products in both the Exercised Countries and other countries in the Territory, the Parties will coordinate license negotiations with such Third Party for rights in both the Exercised Countries and other countries in the Territory.

11.9 **Manner of Royalty Payment.** Each Party will calculate and report royalty payments due by such Party to the other Party under Section 11.3 or 11.5, as applicable, each Calendar Quarter. Each Party shall pay all royalty payments due under Section 11.3 or 11.5, as applicable, within sixty (60) days after the end of each Calendar Quarter and shall include with each payment a report containing the following information for the applicable Calendar Quarter: (a) the amount of gross sales (in U.S. dollars) of the Products in the Territory; (b) an itemized calculation of Net Sales in the Territory showing deductions, to the extent applicable, provided for in the definition of "Net Sales"; (c) a calculation of the royalty payment due on such sales;
(d) an accounting of the number of units and prices for the Products sold; and (e) application of

the reductions, if any, made in accordance with the terms of Section 11.7 and 11.8. Within twenty (20) Business Days after the end of each Calendar Quarter, each Party shall provide a preliminary report as described above for the most recent Calendar Quarter then ended. Each Party shall reasonably cooperate to reconcile any deviations and confirm the accuracy to the extent necessary under Applicable Laws, GAAP or IFRS.

11.10 **Exchange Rate**. The rate of exchange to be used in computing the amount of currency equivalent in U.S. Dollars owed to a Party under this Agreement shall be equal to the weighted average exchange rate, over the applicable Calendar Quarter, between each currency of origin and U.S. Dollars as reported by OANDA (www.oanda.com), or an equivalent resource as agreed by the Parties, on the last Business Day of the Calendar Quarter in which the applicable Net Sales were made.

11.11 **Taxes**

(a) **Cooperation and Coordination**. The Parties acknowledge and agree that it is their mutual objective and intent to appropriately calculate, to the extent feasible and legal, taxes payable with respect to their collaborative efforts under this Agreement and that they shall use all commercially reasonable efforts to cooperate and coordinate with each other to achieve such objective. Ultragenyx shall cooperate with Takeda in seeking any tax exemption or credits that may be available to Takeda with respect to any research which Takeda or its affiliates perform or fund under this Agreement, including any credits under section 45C of the U.S. Internal Revenue Code of 1986, as amended.

(b) **Payment of Tax**. A Party receiving a payment pursuant to this ARTICLE 11 shall pay any and all taxes levied on such payment. A Party making a payment pursuant to this ARTICLE 11 shall make a reasonable effort to obtain the lowest tax rate under Applicable Laws for taxes required to be deducted and withheld. If Applicable Laws require that taxes be deducted and withheld from a payment made pursuant to this ARTICLE 11, after a Party making a payment makes a reasonable effort to obtain the lowest tax rate, the remitting Party shall: (i) deduct those taxes from the payment; (ii) pay the taxes to the proper taxing authority; and (iii) send evidence of the obligation together with proof of payment to the other Party within sixty (60) days following that payment.

(c) **Tax Residence Certificate**. A Party receiving a payment pursuant to this ARTICLE 11 shall provide the remitting Party appropriate certification from relevant revenue authorities that such Party is a tax resident of that jurisdiction, if such receiving Party wishes to claim the benefits of an income tax treaty to which that jurisdiction is a party. Upon the receipt thereof, any deduction and withholding of taxes shall be made at the appropriate treaty tax rate.

(d) **Assessment**. Either Party may, at its own expense, protest any assessment, proposed assessment, or other claim by any Governmental Authority for any additional amount of taxes, interest or penalties or seek a refund of such amounts paid if permitted to do so by Applicable Laws. The Parties shall cooperate with each other in any protest by providing records and such additional information as may reasonably be necessary for a Party to pursue such protest.

(e) **Withholding**. If a Party that owes a payment under this Agreement assigns its rights and obligations to any Person and if, solely as a result of such assignment, the withholding or deduction of tax required by Applicable Laws with respect to payments under this Agreement is increased, then, subject to Section 11.11(f), any amount payable under this Agreement shall be increased to take into account such withheld or deducted taxes as may be necessary so that, after making all required withholdings and deductions (including withholdings and deductions on amounts payable under this Section 11.11(e)), the payee receives an amount equal to the sum it would have received had no such increased withholding or deduction been made. For the avoidance of doubt, if a payee under this Agreement assigns its rights and obligations under this Agreement, the payee shall not be entitled to any additional payments with respect to Taxes arising as a result of such payee's assignment.

(f) **Credit.** To the extent a payee obtains any credit for Taxes for which it has received a payment pursuant to Section 11.11(e) against any liability for tax in the year in which the receipt is taxable, any preceding years, or any succeeding years within the term of this Agreement, thereby reducing out-of-pocket tax payments by the Section 11.11(e)-payee in such year or years, calculated on a "with and without" basis, the Section 11.11(e)-payee shall promptly reimburse the Section 11.11(e)-payor an amount equal to its tax savings resulting from such credit and the Section 11.11(e)-payee shall timely provide the Section 11.11(e)-payor with reasonable evidence as may reasonably be requested to determine whether any amounts are subject to reimbursement pursuant to this Section 11.11(f).

11.12 **Audit.** Each Party will maintain complete and accurate records in sufficient detail to permit the other Party to confirm the accuracy of the calculation of royalty and other payments under this Agreement. Upon reasonable prior notice, such records shall be available during regular business hours for a period of three (3) years from the end of the Calendar Year to which they pertain for examination at the expense of the requesting Party, and not more often than once each Calendar Year, by an independent certified public accountant selected by the requesting Party and reasonably acceptable to the other Party, for the sole purpose of verifying the accuracy of the financial reports furnished by the other Party pursuant to this Agreement. Any such auditor shall not disclose the other Party's Confidential Information, except to the extent such disclosure is necessary to verify the accuracy of the financial reports furnished by the other Party or the amount of payments due by the other Party under this Agreement during the prior thirty six (36) months. Any amounts shown to be owed but unpaid shall be paid within thirty (30) days from the accountant's report, plus interest (as set forth in Section 11.13) from the original due date. Any amounts shown to have been overpaid shall be refunded within thirty (30) days from the accountant's report. The requesting Party shall bear the full cost of such audit unless such audit discloses an underpayment by other Party of more than five percent (5%) of the amount due, in which case the other Party shall bear the full cost of such audit.

11.13 **Manner of Payment, Late Payment.** All payments due to a Party hereunder shall be made in U.S. Dollars by wire transfer of immediately available funds into an account designated by such Party. If a Party does not receive payment of any sum due to it on or before the due date, simple interest shall thereafter accrue on the sum due to such Party until the date of payment at the per annum rate of one percent (1%) over the then-current prime rate quoted by

Citibank in New York City or the maximum rate allowable by Applicable Laws, whichever is lower.

11.14 **Finance and Accounting Working Group**. The Parties shall cooperate with each other to achieve the finance and accounting objectives contemplated herein in a timely, accurate and responsive manner. The Parties shall establish a finance and accounting working group to manage financial and accounting affairs related to the Products, which, for at least the first twelve (12) months after the Effective Date, shall meet monthly unless otherwise agreed upon by the Parties.

ARTICLE 12 – INTELLECTUAL PROPERTY MATTERS

12.1 **Ownership of Inventions**.

(a) **Sole Ownership.** Subject to the terms of this Agreement, each Party shall own any Inventions made solely by its own employees, agents, or independent contractors or its Affiliate's or sublicensees' employees, agents, or independent contractors in the course of conducting its activities under this Agreement, together with all intellectual property rights therein.

(b) **Joint Ownership**. The Parties shall jointly own any Inventions that are made jointly by employees, agents, or independent contractors of each Party or its Affiliates in the course of performing activities under this Agreement, together with all intellectual property rights therein (the "Joint Inventions").

(c) **Inventorship.** For purposes of this Agreement, inventorship shall be determined in accordance with U.S. patent laws.

12.2 **Assignment Obligation and Disclosure of Inventions**.

(a) Each Party shall cause all Persons who perform activities for such Party under this Agreement to be under an obligation to assign (or, if such Party is unable to cause such Person to agree to such assignment obligation despite such Party using commercially reasonable efforts to negotiate such assignment obligation, provide a license under) their rights in any Information and Inventions resulting therefrom to such Party, except where Applicable Law requires otherwise and except in the case of governmental, not-for-profit and public institutions which have standard policies against such an assignment (in which case a suitable license, or right to obtain such a license, shall be obtained).

(b) Takeda will promptly disclose to Ultragenyx in writing, the conception, discovery, development or making of any Joint Inventions and any Inventions Covering Ultragenyx Pipeline Improvements by Persons who perform activities for Takeda under this Agreement.

(c) Ultragenyx will promptly disclose to Takeda in writing the conception, discovery, development or making of any Joint Inventions and any Inventions Covering Licensed Product Improvements, or Option Product Improvements.

(d) Each Party will promptly disclose to the other Party in writing, the conception, discovery, development or making of any Joint Inventions by Persons who perform activities for it under this Agreement.

12.3 **Prosecution of Patents.**

(a) **Licensed** [***] **Patents, Licensed Product Improvement Patents, and Joint Patents relating to Licensed Products.** Except as otherwise provided in this Section 12.3(a), as between the Parties, Takeda shall have the sole right and authority to prepare, file, prosecute and maintain the Licensed [***] Patent, Licensed Product Improvement Patents, and, where relating to Licensed Products, Joint Patents (collectively, the "[***] Patent Prosecution") on a worldwide basis (including the right to defend in patent office proceedings such as inter partes reviews, post grant reviews and oppositions).Takeda shall bear all costs of preparation, filing, prosecution and maintenance of the [***] Patent Prosecution in the Territory. Provided that Ultragenyx's rights with respect to the applicable Licensed Product have not terminated, Takeda, upon Ultragenyx's request, shall provide Ultragenyx a reasonable opportunity to review and comment on material communications from any patent authority in the Territory regarding the [***] Patent Prosecution and drafts of any material filings or responses to be made to such patent authorities in advance of submitting such filings or responses. Takeda shall consider Ultragenyx's comments regarding such communications and drafts in good faith with a view to maximizing the Patent protection and scope in the Territory in the Ultragenyx Field. If Ultragenyx's rights with respect to the applicable Licensed Product have not terminated and Takeda determines in its sole discretion to abandon or not maintain any Licensed [***] Patent, Licensed Product Improvement Patent, or, where relating to Licensed Products, Joint Patent that is being prosecuted or maintained by Takeda in the Territory and that is applicable to the in the Ultragenyx Field, then Takeda shall provide Ultragenyx with written notice of such determination within a period of time reasonably necessary to allow Ultragenyx to determine, in its sole discretion, its interest in such Patent(s) (which notice by Takeda shall be given no later than sixty (60) days prior to the final deadline for any pending action or response that may be due with respect to such Patent(s) with the applicable patent authority). If Ultragenyx provides timely written notice expressing its interest in continuing to support such Patent(s), Ultragenyx shall have the right to pursue the filing or support the continued prosecution or maintenance of such Patents and Takeda shall provide to Ultragenyx, subject to reimbursement of Takeda's out-of-pocket costs, all unpublished patent applications and any other information and documents necessary to permit Ultragenyx to take such action to establish or preserve any such Patents. If Ultragenyx pursues the filing or support of such Patents and Takeda continues to pursue a Licensed [***] Product in the Takeda Field, it shall provide Takeda a reasonable opportunity to review and comment on material communications from any patent authority in the Territory regarding such Patents and drafts of any material filings or responses to be made to such patent authorities in advance of submitting such filings or responses. Ultragenyx shall consider Takeda's comments regarding such communications and drafts in good faith.

(b) **Option Product Patents, Option Product Improvement Patents, and Joint Patents Relating to Research Products.** Except as otherwise provided in this Section 12.3(b), as between the Parties, Takeda shall have the sole right and authority to prepare, file, prosecute and maintain the Option Product Patents, Option Product Improvement Patents and, where relating to Research Products, Joint Patents on a worldwide basis (including the right to defend in patent office proceedings such as inter partes reviews, post grant reviews and oppositions). Takeda shall bear all costs of preparation, filing, prosecution and maintenance of Option Product Patents, Option Product Improvement Patents and, where relating to Research Products, Joint Patents in the Territory. During the Collaboration Term, Takeda, upon Ultragenyx's request, shall provide Ultragenyx a reasonable opportunity to review and comment on material communications from any patent authority in the Territory regarding Option Product Patents, Option Product Improvement Patents and, where relating to Research Products, Joint Patents and drafts of any material filings or responses to be made to such patent authorities in advance of submitting such filings or responses. Takeda shall consider Ultragenyx's comments regarding such communications and drafts in good faith with a view to maximizing the Patent protection and scope in the Territory in the Licensed Field; provided that final decision making authority rests with Takeda. If, during the Collaboration Term, Takeda determines in its sole discretion to abandon or not maintain any Option Product Patent, Option Product Improvement Patent and, where relating to Research Products, Joint Patent that is being prosecuted or maintained by Takeda in the Territory, then Takeda shall provide Ultragenyx with written notice of such determination within a period of time reasonably necessary to allow Ultragenyx to determine, in its sole discretion, its interest in such Patent(s) (which notice by Takeda shall be given no later than sixty (60) days prior to the final deadline for any pending action or response that may be due with respect to such Patent(s) with the applicable patent authority). If Ultragenyx provides timely written notice expressing its interest in continuing to support such Patent(s), Ultragenyx shall have the right to pursue the filing or support the continued prosecution or maintenance of such Patents and Takeda shall provide to Ultragenyx, subject to reimbursement of Takeda's out- of-pocket costs, all unpublished patent applications and any other information and documents necessary to permit Ultragenyx to take such action to establish or preserve any such Patents. If Ultragenyx pursues the filing or support of such Patents, it shall provide Takeda a reasonable opportunity to review and comment on material communications from any patent authority in the Territory regarding such Patents and drafts of any material filings or responses to be made to such patent authorities in advance of submitting such filings or responses. Ultragenyx shall consider Takeda's comments regarding such communications and drafts in good faith. Notwithstanding the foregoing, following the execution of an Option Product License Agreement and/or Exercised Product License Agreement covering an Option Product, the terms of such license agreement(s) shall govern the handling of the preparation, filing, prosecution and maintenance of Patents covering the Option Product(s).

(c) **Ultragenyx Pipeline Patents, Ultragenyx Pipeline Improvement Patents, Ultragenyx** [***] **Patents and Joint Patents Related to Ultragenyx Pipeline Products**. Except as otherwise provided in this Section 12.3(c), as between the Parties, Ultragenyx shall have the sole right and authority to prepare, file, prosecute and maintain the Ultragenyx Pipeline Patents, Ultragenyx Pipeline Improvement Patents, Ultragenyx [***] Patents and, where relating to Ultragenyx Pipeline Products, the Patents included in the Joint Inventions (the "Joint Patents"),

on a worldwide basis (including the right to defend in patent office proceedings such as inter partes reviews, post grant reviews and oppositions). Ultragenyx shall bear all costs of preparation, filing, prosecution and maintenance of Ultragenyx Pipeline Patents, Ultragenyx Pipeline Improvement Patents, Ultragenyx [***] Patents and, where relating to Ultragenyx Pipeline Products, Joint Patents in the Territory. During the Takeda Option Term, Ultragenyx, upon Takeda's request, shall provide Takeda a reasonable opportunity to review and comment on material communications from any patent authority in the Territory regarding Ultragenyx Pipeline Patents, Ultragenyx Pipeline Improvement Patents, Ultragenyx [***] Patents and, where relating to Ultragenyx Pipeline Products, Joint Patents and drafts of any material filings or responses to be made to such patent authorities in advance of submitting such filings or responses. Ultragenyx shall consider Takeda's comments regarding such communications and drafts in good faith with a view to maximizing the Patent protection and scope in the Territory; provided that final decision making authority rests with Ultragenyx. During the Takeda Option Term, if Ultragenyx determines in its sole discretion to abandon or not maintain any Ultragenyx Pipeline Patent, Ultragenyx Pipeline Improvement Patent, Ultragenyx [***] Patent and, where relating to Ultragenyx Pipeline Products, Joint Patent that is being prosecuted or maintained by Ultragenyx in the Takeda Territory, then Ultragenyx shall provide Takeda with written notice of such determination within a period of time reasonably necessary to allow Takeda to determine, in its sole discretion, its interest in such Patent(s) (which notice by Ultragenyx shall be given no later than sixty (60) days prior to the final deadline for any pending action or response that may be due with respect to such Patent(s) with the applicable patent authority). If Takeda provides timely written notice expressing its interest in continuing to support such Patent(s), Takeda shall have the right to pursue the filing or support the continued prosecution or maintenance of such Patents and Ultragenyx shall provide to Takeda, subject to reimbursement of Ultragenyx's out- of-pocket costs, all unpublished patent applications and any other information and documents necessary to permit Takeda to take such action to establish or preserve any such Patents. If Takeda pursues the filing or support of such Patents, it shall provide Ultragenyx a reasonable opportunity to review and comment on material communications from any patent authority in the Territory regarding such Patents and drafts of any material filings or responses to be made to such patent authorities in advance of submitting such filings or responses. Takeda shall consider Takeda's comments regarding such communications and drafts in good faith. Notwithstanding the foregoing, following the execution of an Exercised Product License Agreement covering an Ultragenyx Pipeline Product, the terms of such license agreement shall govern the handling of the preparation, filing, prosecution and maintenance of Patents covering such Ultragenyx Pipeline Product.

(d) **Cooperation in Prosecution**. Each Party shall provide the other Party all reasonable assistance and cooperation in the Patent prosecution efforts provided above in this Section 12.3, including providing any necessary powers of attorney and executing any other required documents or instruments for such prosecution, as well as further actions as set forth below.

(i) The Parties shall respectively prepare, file, maintain and prosecute the Patents as set forth in this Section 12.3. As used herein, "prosecution" of such Patents shall

include all communication and other interaction with any patent office or patent authority having jurisdiction over a patent application in connection with pre-grant proceedings.

(ii) All communications between the Parties relating to the preparation, filing, prosecution or maintenance of the Patents as set forth in this Section 12.3, including copies of any draft or final documents or any communications received from or sent to patent offices or patenting authorities with respect to such Patents, shall be considered Confidential Information and subject to the confidentiality provisions of ARTICLE 14.

12.4 **Patent Term Extensions in the Territory**.

(a) The Parties will discuss and approve for which, if any, of the Patents under this Agreement the Parties should seek Patent Term Extensions in the Territory**.** If the Parties are unable to reach agreement for which, if any, of such Patents the Parties should seek Patent Term Extension, the final decision shall rest with the Party who first receives Regulatory Approval for the Licensed Product or Option Product, as applicable, with respect to which the Patent Term applies for such Party's territory. The Party with final decision-making authority shall act with reasonable promptness in light of the stage of the Products to apply for any such Patent Term Extensions, in accordance with such decision. The Party that does not apply for an extension hereunder will cooperate fully with the other Party in making such filings or actions, including making available all required Regulatory Materials (including underlying data) and Information and executing any required authorizations to apply for such Patent Term Extension. All expenses incurred in connection with activities of each Party with respect to the Patent(s) for which such Party seeks Patent Term Extensions pursuant to this 12.4 shall be entirely borne by the Party applying for such Patent Term Extension.

12.5 **Orange Book Listing**. The Party that is the NDA holder for the applicable Product shall be responsible for listing and maintaining all applicable Patents in the Orange Book**,** including payment of all costs and expenses related to such maintenance incurred after the Effective Date. The listing and maintaining Party shall provide the other Party with its planned listings in advance of their submission with sufficient time for the other Party to review and provide comments. The listing and maintaining Party shall consider any such comments in good faith. Upon request of the listing and maintaining Party, the other Party shall cooperate in the filing of appropriate information with the FDA listing such Patents in the Orange Book.

12.6 **Infringement of Patents by Third Parties**.

(a) **Notification**. Each Party shall promptly notify the other Party in writing of any existing, alleged or threatened infringement of the Licensed [***] Patents, Licensed Product Improvement Patents, Ultragenyx [***] Patents, Option Product Patents, Option Product Improvement Patents, Ultragenyx Pipeline Patents, Ultragenyx Pipeline Improvement Patents, and Joint Patents in the Licensed Field in the Territory of which it becomes aware, and shall provide all Information in such Party's possession or control demonstrating such infringement.

(b) **Infringement Action**.

(i) Takeda shall have the first right, but not the obligation, to bring an appropriate suit or other action against any Third Party engaged in any existing, alleged or threatened infringement related to the Joint Patents, Licensed [***] Patents, Licensed Product Improvement Patents, Ultragenyx [***] Patents, Option Product Patents, and Option Product Improvement Patents, in each case where relating to Licensed Products or Research Products (a "Takeda Product Infringement"), subject to Section 12.6(b)(ii) through 12.6(b)(iv); provided that if a Takeda Product Infringement concerns the enforcement of any Valid Claim against a Third Party making, using, selling, offering for sale, or importing solely within the Ultragenyx Field, Takeda must receive Ultragenyx's prior consent with respect to all strategic decisions in connection with such Takeda Product Infringement, such consent not to be unreasonably withheld, conditioned, or delayed; and provided further that if Takeda is not Developing or Commercializing the Licensed [***] Product in the Takeda Field, then the foregoing first right with respect to a Takeda Product Infringement shall become Ultragenyx's first right hereunder. Ultragenyx shall have the first right, but not the obligation, to bring an appropriate suit or other action against any Third Party engaged in any existing, alleged or threatened infringement related to the Joint Patents, Ultragenyx Pipeline Patents and Ultragenyx Pipeline Improvement Patents, in each case where relating to an Ultragenyx Pipeline Product (an "Ultragenyx Product Infringement"), subject to Section 12.6(b)(ii) through 12.6(b)(iv). Notwithstanding the foregoing, following the execution of an Option Product License Agreement or Exercised Product License Agreement, the terms of such license agreement shall govern the handling of the infringement actions relating to the Patents covering such Licensed Option Product or Exercised Product, respectively, that is the subject of such license agreement.

(ii) The Parties shall discuss how to address each Takeda Product Infringement and Ultragenyx Product Infringement and the Party with the first right to enforce shall consider in good faith the input of the other Party in determining how to proceed. The Party with the first right to enforce shall notify the other Party of its election to take any action in accordance with Section 12.6(b)(i) within ten (10) Business Days before any time limit set forth in an Applicable Laws or regulation, including the time limits set forth under the Hatch Waxman Act. In the event such Party does not so elect, it shall so notify the other Party in writing, and the other Party shall have the right to commence a suit or take action to enforce the applicable Patent against such Third Party perpetrating such Takeda Product Infringement or Ultragenyx Product Infringement, as applicable, in the applicable portion of the Territory at its own cost and expense. If one Party elects to bring suit or take action against the Takeda Product Infringement or Ultragenyx Product Infringement, as applicable, then the other Party (at its expense) shall have the right, prior to commencement of the trial, suit or action, to join any such suit or action.

(iii) Each Party shall provide to the Party enforcing any such rights under this Section 12.6(b) reasonable assistance in such enforcement, at such enforcing Party's request and expense, including joining such action as a party plaintiff if required by Applicable Laws to pursue such action. The enforcing Party shall keep the other Party regularly informed of the status and progress of such enforcement efforts and shall reasonably consider the other Party's comments on any important aspects of such enforcement, including determination of litigation strategy and filing of important papers to the competent court.

(iv) Subject to this Section 12.6(b)(iv), the enforcing Party shall be solely responsible for all costs and expenses arising from a suit or action against a Takeda Product Infringement or Ultragenyx Product Infringement, as applicable. For the avoidance of doubt, the enforcing Party shall not be responsible for the other Party's internal costs (e.g., FTEs) incurred as a result of the other Party's cooperation with the enforcement action as provided in Section 12.6(b)(iii). The Party not bringing an action with respect to the Takeda Product Infringement or Ultragenyx Product Infringement, as applicable, under this Section 12.6(b) shall be entitled to separate representation in such matter by counsel of its own choice and at its own expense, but such Party shall at all times cooperate fully with the Party bringing such action.

(c) **Settlement**. The enforcing Party may settle any claim, suit or action that it has brought under this Section 12.6 without the prior written consent of the other Party; provided that any such settlement does not negatively impact the non-enforcing Party's rights or interests in such non-enforcing Party's territory or field.

(d) **Allocation of Proceeds**. If either Party recovers monetary damages from any Third Party in a suit or action brought under Sections 12.6(b), 12.6(c), or 12.8(b) or any royalties from a license agreement with a Third Party related to any alleged Takeda Product Infringement or Ultragenyx Product Infringement, as applicable, such recovery shall be allocated first to the reimbursement of any expenses incurred by the Parties in such suit or action, and any remaining amounts shall be split as follows: (i) if such suit or action is initiated or defended by Ultragenyx, such amounts shall be retained by Ultragenyx, or (ii) if such suit or action was initiated or defended by Takeda, such amounts shall be retained by Takeda.

12.7 **Infringement of Third Party Rights in the Territory**.

(a) **Notice**. If any Licensed Product used or sold by either Party, its Affiliates, licensees or sublicensees becomes the subject of a Third Party's claim or assertion of infringement of a Patent granted in either Party's field or territory, the Party first having notice of the claim or assertion shall promptly notify the other Party, the Parties shall agree on and enter into an "identity of interest agreement" wherein such Parties agree to their shared, mutual interest in the outcome of such potential dispute, and thereafter, the Parties shall promptly meet to consider the claim or assertion and the appropriate course of action.

(b) **Defense**.

(i) Ultragenyx shall have the first right, but not the obligation, to defend any Third Party claim or assertion of infringement of a Patent described in Section 12.7(a) above by Ultragenyx Pipeline Products, at Ultragenyx's expense. If Ultragenyx does not commence actions to defend such claim within thirty (30) days after it receives notice thereof (or within thirty (30) days after it should have given notice thereof to Takeda as required by Section 12.7(a)), then, to the extent allowed by Applicable Laws, Takeda shall have the right, but not the obligation, to control the defense of such claim by counsel of its choice, at Takeda's expense. The non-defending Party shall reasonably cooperate with the Party conducting the defense of the claim or assertion, including if required to conduct such defense, furnishing a power of attorney.

(ii) Takeda shall have the first right, but not the obligation, to defend any Third Party claim or assertion of infringement of a Patent described in Section 12.7(a) above by Licensed [***] Products, Licensed Analog Products, Candidate Products or Option Products, at Takeda's expense. If Takeda does not commence actions to defend such claim within thirty (30) days after it receives notice thereof (or within thirty (30) days after it should have given notice thereof to Ultragenyx as required by Section 12.7(a)), then, to the extent allowed by Applicable Laws, Ultragenyx shall have the right, but not the obligation, to control the defense of such claim by counsel of its choice, at Ultragenyx's expense. The non-defending Party shall reasonably cooperate with the Party conducting the defense of the claim or assertion, including if required to conduct such defense, furnishing a power of attorney.

(iii) Notwithstanding the foregoing, following the execution of an Option Product License Agreement or Exercised Product License Agreement, the terms of such license agreement shall govern the handling of the defense against infringement by Product(s) that are the subject of the applicable license agreement.

(c) **Settlement; Licenses**. Neither Party shall enter into any settlement of any claim described in this Section 12.7 that negatively affects the other Party's rights or interests without such other Party's written consent, which consent shall not be unreasonably withheld, conditioned or delayed. Each Party shall have the right to decline to defend or to tender defense of any such claim to the other Party upon reasonable notice, including if the other Party fails to agree to a settlement that such Party proposes. In the event that it is determined by any court of competent jurisdiction that the Exploitation of a Product in the Licensed Field in the Ultragenyx Territory, conducted in accordance with the terms and conditions of this Agreement, infringes, or the JSC determines that such activities are likely to infringe, any patent, copyright, trademark, data exclusivity right or trade secret right arising under Applicable Laws of any Third Party, Ultragenyx shall use Commercially Reasonable Efforts to: (i) procure a license from such Third Party authorizing Ultragenyx to continue to conduct such activities; or (ii) modify such activities so as to render it non-infringing.

12.8 **Patent Oppositions and Other Proceedings**.

(a) **Third-Party Patent Rights**. If either Party desires to bring an opposition, action for declaratory judgment, nullity action, interference, declaration for non-infringement, reexamination or other attack upon the validity, title or enforceability of a Patent owned or controlled by a Third Party and having one or more claims that covers a Product, or the use, sale, offer for sale or importation of a Product (except insofar as such action is a counterclaim to or defense of, or accompanies a defense of, a Third Party's claim or assertion of infringement under Section 12.7, in which case the provisions of Section 12.7 shall govern), such Party shall so notify the other Party and the Parties shall promptly confer to determine whether to bring such action or the manner in which to settle such action. Ultragenyx shall have the exclusive right, but not the obligation, to bring at its own expense and in its sole control such action in the Territory with respect to Ultragenyx Pipeline Products. Takeda shall have the exclusive right, but not the obligation, to bring at its own expense and in its sole control such action with respect to Licensed [***] Products, Licensed Analog Products and Research Products in the Territory. If the

Party with the first right does not bring such an action, within ninety (90) days of notification thereof pursuant to this Section 12.8(a) (or earlier, if required by the nature of the proceeding), then the other Party shall have the right, but not the obligation, to bring, at its sole expense, such action. The Party not bringing an action under this Section 12.8(a) shall be entitled to separate representation in such proceeding by counsel of its own choice and at its own expense, and shall cooperate fully with the Party bringing such action. Any awards or amounts received in bringing any such action shall be first allocated to reimburse the initiating Party's expenses in such action and any remaining amounts shall be retained by such Party.

(b) **Parties' Patent Rights**. If any Licensed [***] Patents, Licensed Product Improvement Patent, Ultragenyx [***] Patents, Option Product Patent, Option Product Improvement Patent, Ultragenyx Pipeline Patent, Ultragenyx Pipeline Improvement Patent, or Joint Patent becomes the subject of any proceeding commenced by a Third Party within the Territory in connection with an opposition, reexamination request, action for declaratory judgment, nullity action, interference or other attack upon the validity, title or enforceability thereof (except insofar as such action is a counterclaim to or defense of, or accompanies a defense of, an action for infringement against a Third Party under Section 12.6, in which case the provisions of Section 12.6 shall govern), then the Party responsible for filing, preparing, prosecuting and maintaining such Patent as set forth in Section 12.3, shall control such defense at its own cost and expense. The controlling Party shall permit the non-controlling Party to participate in the proceeding to the extent permissible under Applicable Laws, and to be represented by its own counsel in such proceeding, at the non-controlling Party's expense. If the controlling Party decides that it does not wish to defend against such action, then the other Party shall have a backup right to assume defense of such Third-Party action at its own expense. Any awards or amounts received in defending any such Third-Party action shall be allocated between the Parties as provided in Section 12.6(d).

ARTICLE 13 – REPRESENTATIONS AND WARRANTIES

13.1 **Mutual Representations, Warranties and Covenants**. Each of the Parties hereby represents and warrants to the other Party as of the Execution Date and covenants that:

(a) **Organization.** It is a corporation duly organized, validly existing, and in good standing under the laws of the jurisdiction of its organization, and has all requisite power and authority, corporate or otherwise, to execute, deliver, and perform this Agreement.

(b) **Binding Agreement.** This Agreement is a legal and valid obligation binding upon such Party and enforceable in accordance with its terms, subject to the effects of bankruptcy, insolvency, or other laws of general application affecting the enforcement of creditor rights, judicial principles affecting the availability of specific performance, and general principles of equity (whether enforceability is considered a proceeding at law or equity).

(c) **Authorization.** The execution, delivery, and performance of this Agreement by such Party have been duly authorized by all necessary corporate action and do not conflict with any agreement, instrument, or understanding, oral or written, to which it is a party or by which it is bound, nor violate any Applicable Laws or any order, writ, judgment, injunction, decree,

determination, or award of any court or governmental body, or administrative or other agency presently in effect applicable to such Party.

(d) **No Further Approval.** Subject to Section 18.1, it is not aware of any government authorization, consent, approval, license, exemption of or filing or registration with any court or governmental department, commission, board, bureau, agency or instrumentality, domestic or foreign, under any Applicable Laws, currently in effect, necessary for, or in connection with, the transactions contemplated by this Agreement or any other agreement or instrument executed in connection herewith, or for the performance by it of its obligations under this Agreement and such other agreements (save for Regulatory Approvals and similar authorizations from Regulatory Authorities necessary for the Exploitation of the Compounds and the Products as contemplated hereunder).

(e) **No Inconsistent Obligations.** Neither Party is under any obligation, contractual or otherwise, to any Person that conflicts with or is inconsistent in any material respect with the terms of this Agreement, or that would impede the diligent and complete fulfillment of its obligations hereunder.

(f) **Transparency Reporting**. Each Party shall be responsible for tracking and reporting transfers of value initiated and controlled by its and its Affiliates' employees, independent contractors, and agents pursuant to the requirements of the marketing reporting laws of any Government Authority in the Territory, including Section 6002 of the Patient Protection and Affordable Care Act, commonly referred to as the "Sunshine Act."

(g) Neither Party nor any of its Affiliates has been debarred by the FDA, is subject to any similar sanction of other Regulatory Authorities in the Territory, and neither Party nor any of its Affiliates has used, or will engage, in any capacity, in connection with this Agreement or any ancillary agreements (if any), any Person who either has been debarred by such a Regulatory Authority, or is the subject of a conviction described in Section 306 of the FFDCA. Each Party shall inform the other in writing promptly if it or any Person engaged by such Party or any of its Affiliates who is performing services under this Agreement or any ancillary agreements (if any) is debarred or is the subject of a conviction described in Section 306 of the FFDCA, or if any action, suit, claim, investigation or legal or administrative proceeding is pending or, to such Party's Knowledge, is threatened, relating to the debarment or conviction of such Party, any of its Affiliates or any such Person performing services hereunder or thereunder.

13.2 **Additional Representations, Warranties and Covenants of Takeda**. Takeda represents and warrants as of the Execution Date and covenants to Ultragenyx that:

(a) Takeda has all rights necessary to grant the options and licenses under the Licensed [***] Technology and Option Product Technology and rights of cross-reference under Regulatory Materials, in each case, existing as of the Execution Date that it grants to Ultragenyx in this Agreement. For the duration of the Term, Takeda shall not, and shall cause its Affiliates not to, grant to any Third Party rights in the Licensed Field or the Ultragenyx Field, as applicable, in the Territory that encumber, diminish or conflict with the rights granted to

Ultragenyx hereunder with respect to the Licensed [***] Technology, Option Product Technology, Joint Intellectual Property or Regulatory Materials.

(b) (i) The Patents set forth in Exhibit 1.168 represent all Takeda Patents, (ii) to Takeda's Knowledge, the Compounds set forth in Exhibit 13.2(b) represent all structures Controlled by Takeda that are [***], and (i) to Takeda's Knowledge, the Compound set forth in Exhibit 1.94 represents the sole Licensed [***] Compound. Takeda (Y) is the sole and exclusive owner of the entire right, title and interest in the Takeda Patents, and (Z) to Takeda's Knowledge, the sole and exclusive owner of the entire right, title and interest in the Licensed [***] Compound and Licensed Analog Compounds, and in each of cases (Y) and (Z), free of any encumbrance, lien, or claim of ownership by any Third Party.

(c) To Takeda's Knowledge, there is no actual or threatened infringement or misappropriation of the Licensed [***] Technology and Option Product Technology by any Person in the Territory.

(d) The Takeda Patents are being diligently prosecuted in the Territory in accordance with Applicable Laws. To Takeda's Knowledge, the Takeda Patents have been filed and maintained properly and correctly and all applicable fees have been paid on or before the due date for payment.

(e) To Takeda's Knowledge, each of the Takeda Patents properly identifies each and every inventor of the claims thereof as determined in accordance with Applicable Laws of the jurisdiction in which such Takeda Patent is issued or such application is pending.

(f) To the extent permissible under Applicable Laws, all employees of Takeda or its Affiliates performing activities under this Agreement are and shall be under an obligation to assign all right, title and interest in and to their Inventions and intellectual property rights therein, to Takeda or its Affiliate(s) as the sole owner thereof. Ultragenyx shall have no obligation to contribute to any remuneration of any inventor employed or previously employed by Takeda or any of its Affiliates in respect of any such Inventions and intellectual property rights therein that are so assigned to Takeda or its Affiliate(s). Takeda will pay all such remuneration due to such inventors with respect to such Inventions and intellectual property rights therein.

(g) The Inventions claimed or disclosed by the Takeda Patents (i) were not conceived, discovered, developed, or otherwise made in connection with any research activities funded, in whole or in part, by the federal government of the U.S. or any agency thereof, (ii) are not a "subject invention" as that term is described in 35 U.S.C. Section 201(f), and (iii) are not otherwise subject to the provisions of the Bayh-Dole Act.

(h) To Takeda's Knowledge, there are no material claims, judgments, or settlements against, or amounts with respect thereto, owed by Takeda or any of its Affiliates to any Third Parties relating to the Regulatory Materials, Licensed [***] Technology or Option Product Technology in the Territory.

(i) No claim or litigation in the Territory has been brought or, to Takeda's Knowledge, threatened by any Person alleging, and Takeda has no Knowledge of any claim, whether or not asserted: (i) that any of the Takeda Patents is invalid or unenforceable, (ii) that the Regulatory Materials, or the disclosing, copying, making, assigning, or licensing of the Regulatory Materials, violates, infringes, or otherwise conflicts or interferes with, or would violate, infringe, or otherwise conflict or interfere with, any intellectual property or proprietary right of any Person; or (iii) related to the Development or Commercialization of the Licensed Products or Research Products, including any claims of Product Liability.

(j) Takeda has no Knowledge of any material adverse information with respect to the safety and efficacy of any Licensed Product or Research Product that has not been disclosed to Ultragenyx, and all such information that has been disclosed is true, correct, and complete in all material respects.

(k) To Takeda's Knowledge, Takeda and its Affiliates have generated, prepared, maintained, and retained all material Regulatory Materials in the Licensed Field that are required to be maintained or retained pursuant to and in accordance with GCP, GLP and other Applicable Laws, and all such information is true, complete and correct in all material respects and what it purports to be.

(l) Takeda**,** without the prior written consent of Ultragenyx, during the Term, will not solicit, induce, encourage, or participate in soliciting, inducing, or encouraging any employee of Ultragenyx, or any of its Affiliates, to terminate his or her relationship with Ultragenyx or Ultragenyx's Affiliate. An offer of employment to an employee of Ultragenyx by Takeda which results directly from unsolicited responses to general advertisements for employment will not be deemed to be in violation of this provision.

(m) In performing its obligations under this Agreement, Takeda shall, and shall cause its Affiliates to, comply with all Applicable Laws, including any applicable anti-corruption or anti-bribery laws or regulation, of any Governmental Authority with jurisdiction over the activities performed by Takeda or its Affiliates in furtherance of such obligations.

13.3 **Additional Representations, Warranties and Covenants of Ultragenyx**. Ultragenyx represents and warrants as of the Execution Date and covenants to Takeda that:

(a) Ultragenyx and its Affiliates have provided or made available to Takeda prior to the Execution Date, true, complete, and correct copies (as of the Execution Date) of all Ultragenyx In-License Agreements.

(b) Ultragenyx has all rights applicable necessary to grant the options and licenses under the Ultragenyx Intellectual Property and rights of cross-reference under Regulatory Materials, in each case, that it grants to Takeda in this Agreement. For the duration of the Term, Ultragenyx shall not, and shall cause its Affiliates not to, grant to any Third Party rights in the Takeda Field in the Territory or the Licensed Field in the Takeda Territory, as applicable, that encumber, diminish or conflict with the rights granted to Takeda hereunder with respect to the Ultragenyx Intellectual Property, Joint Intellectual Property or Regulatory Materials.

(c) The Patents set forth in Exhibit 1.188 represent all Ultragenyx Patents. Ultragenyx is the sole and exclusive owner of the entire right, title and interest in the Ultragenyx Patents free of any encumbrance, lien, or claim of ownership by any Third Party.

(d) To Ultragenyx's Knowledge, there is no actual or threatened infringement or misappropriation of the Ultragenyx Intellectual Property by any Person in the Territory.

(e) The Ultragenyx Patents are being diligently prosecuted in the Territory in accordance with Applicable Laws and consistent with Ultragenyx's current prosecution practices. To Ultragenyx's Knowledge, the Ultragenyx Patents have been filed and maintained properly and correctly and all applicable fees have been paid on or before the due date for payment.

(f) To Ultragenyx's Knowledge, each of the Ultragenyx Patents properly identifies each and every inventor of the claims thereof as determined in accordance with Applicable Laws of the jurisdiction in which such Ultragenyx Patent is issued or such application is pending.

(g) To the extent permissible under Applicable Laws, all employees of Ultragenyx or its Affiliates performing activities under this Agreement shall be under an obligation to assign all right, title and interest in and to their Inventions, and intellectual property rights therein, to Ultragenyx or its Affiliate(s) as the sole owner thereof. Takeda shall have no obligation to contribute to any remuneration of any inventor employed or previously employed by Ultragenyx or any of its Affiliates in respect of any such inventions, Information and discoveries and intellectual property rights therein that are so assigned to Ultragenyx or its Affiliate(s). Ultragenyx will pay all such remuneration due to such inventors with respect to such Inventions and intellectual property rights therein.

(h) To Ultragenyx's Knowledge, the Inventions claimed or disclosed by the Ultragenyx Patents (i) were not conceived, discovered, developed, or otherwise made in connection with any research activities funded, in whole or in part, by the federal government of the U.S. or any agency thereof, (ii) are not a "subject invention" as that term is described in 35 U.S.C. Section 201(f), and (iii) are not otherwise subject to the provisions of the Bayh-Dole Act.

(i) To Ultragenyx's Knowledge, there are no material claims, judgments, or settlements against, or amounts with respect thereto, owed by Ultragenyx or any of its Affiliates to any Third Parties relating to the Regulatory Materials or the Ultragenyx Intellectual Property in the Territory.

(j) Ultragenyx has no Knowledge of any material adverse information with respect to the safety and efficacy of any Compound or Product that has not been disclosed to Takeda, and all such information that has been disclosed is true, correct, and complete in all material respects.

(k) No claim or litigation in the Territory has been brought or, to Ultragenyx's Knowledge, threatened by any Person alleging, and Ultragenyx has no Knowledge of any claim, whether or not asserted: (i) that any of the Ultragenyx Patents is invalid or unenforceable, (ii) that the Regulatory Materials, the Ultragenyx Intellectual Property, or the disclosing, copying,

making, assigning, or licensing of the Regulatory Materials or the Ultragenyx Intellectual Property, violates, infringes, or otherwise conflicts or interferes with, or would violate, infringe, or otherwise conflict or interfere with, any intellectual property or proprietary right of any Person; or (iii) related to the Development or Commercialization of the Products, including any claims of Product Liability.

(l) In performing its obligations under this Agreement Ultragenyx shall, and shall cause its Affiliates to, comply with all Applicable Laws, including any applicable anti-corruption or anti-bribery laws or regulation, of any Governmental Authority with jurisdiction over the activities performed by Ultragenyx or its Affiliates in furtherance of such obligations.

(m) Ultragenyx**,** without the prior written consent of Takeda, during the Term, will not solicit, induce, encourage, or participate in soliciting, inducing, or encouraging any employee of Takeda, or any of its Affiliates, to terminate his or her relationship with Takeda or Takeda's Affiliate. An offer of employment to an employee of Takeda by Ultragenyx which results directly from unsolicited responses to general advertisements for employment will not be deemed to be in violation of this provision.

(n) [***].

(o) Ultragenyx has provided Takeda with true and correct copies (as of the Execution Date) of all Ultragenyx In-License Agreements in effect as of the Execution Date. None of Ultragenyx, its Affiliates and, to their Knowledge, any Third Party, is in breach of any Ultragenyx In-License Agreement and none of Ultragenyx, its Affiliates and, to their Knowledge, any other party to any Ultragenyx In-License Agreement has threatened to terminate, or has otherwise alleged any material breach under, such agreement and each Ultragenyx In-License Agreement is in full force and effect in accordance with its terms

13.4 **No Other Representations or Warranties**. EXCEPT AS EXPRESSLY SET FORTH IN THIS ARTICLE 13, THE PARTIES MAKE NO REPRESENTATIONS OR WARRANTIES OF ANY KIND WHATSOEVER, EITHER EXPRESS OR IMPLIED, WRITTEN OR ORAL, EITHER IN FACT OR BY OPERATION OF LAW, BY STATUTE OR OTHERWISE, AND EACH PARTY SPECIFICALLY DISCLAIMS ANY OTHER WARRANTIES, INCLUDING ANY EXPRESS OR IMPLIED WARRANTY OF QUALITY, MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, OR WARRANTY OF NON-INFRINGEMENT OR AS TO THE VALIDITY OF ANY PATENTS IN THE TERRITORY.

ARTICLE 14 – CONFIDENTIALITY

14.1 **Nondisclosure.** Each Party agrees that, during the Term and for a period of ten (10) years thereafter, a Party (the "Receiving Party") receiving Confidential Information of the other Party (the "Disclosing Party") shall (a) maintain in confidence such Confidential Information using not less than the efforts such Receiving Party uses to maintain in confidence its own confidential or proprietary Information of similar kind and value, (b) not disclose such

Confidential Information to any Third Party without the prior written consent of the Disclosing Party, except for disclosures expressly permitted below, and (c) not use such Confidential Information for any purpose except those permitted by this Agreement (it being understood that this Section 14.1 shall not create or imply any rights or licenses not expressly granted under this Agreement). Notwithstanding anything to the contrary in the foregoing, the obligations of confidentiality and non-use with respect to any trade secret within such Confidential Information shall survive such ten (10) year period for so long as such Confidential Information remains protected as a trade secret under Applicable Laws.

14.2 **Exceptions.** The obligations in Section 14.1 shall not apply with respect to any portion of the Confidential Information that the Receiving Party can show by competent evidence:

(a) is publicly disclosed by the Disclosing Party, either before or after it is disclosed to the Receiving Party hereunder;

(b) is known to the Receiving Party or any of its Affiliates, without any obligation to keep it confidential or any restriction on its use, prior to disclosure by the Disclosing Party;

(c) is subsequently disclosed to the Receiving Party or any of its Affiliates on a non- confidential basis by a Third Party that, to the Receiving Party's Knowledge, is not bound by a similar duty of confidentiality or restriction on its use;

(d) is now, or hereafter becomes, through no act or failure to act on the part of the Receiving Party or any of its Affiliates, generally known or available, either before or after it is disclosed to the Receiving Party;

(e) is independently discovered or developed by or on behalf of the Receiving Party or any of its Affiliates without the use of or access to Confidential Information belonging to the Disclosing Party; or

(f) is the subject of written permission to disclose provided by the Disclosing Party.

14.3 **Authorized Disclosure.** The Receiving Party may disclose Confidential Information belonging to the Disclosing Party only to the extent such disclosure is reasonably necessary in the following instances: filing or prosecuting Patents as permitted by this Agreement;

(b) filing Regulatory Materials in order to obtain or maintain Regulatory Approvals;

(c) prosecuting or defending litigation, including responding to a subpoena in a Third Party litigation;

(d) complying with Applicable Laws or regulations or court or administrative orders;
or

(e) to its Affiliates, sublicensees or prospective sublicensees, subcontractors or prospective subcontractors, payors, consultants, agents and advisors on a "need-to-know" basis

in order for the Receiving Party to exercise its rights or fulfill its obligations under this Agreement, each of whom prior to disclosure must be bound by obligations of confidentiality and restrictions on use of such Confidential Information that are no less restrictive than those set forth in this ARTICLE 14; provided, however, that, in each of the above situations, the Receiving Party shall remain responsible for any failure by any Person who receives Confidential Information pursuant to this Section 14.3 to treat such Confidential Information as required under this ARTICLE 14.

(f) If and whenever any Confidential Information is disclosed in accordance with this Section 14.3, such disclosure shall not cause any such information to cease to be Confidential Information except to the extent that such disclosure results in a public disclosure of such information (other than by breach of this Agreement). Notwithstanding the foregoing, in the event a Party is required to make a disclosure of the other Party's Confidential Information pursuant to clauses (a) through (d) of this Section 14.3, it will, except where impracticable, give reasonable advance notice to the other Party of such disclosure and use not less than the same efforts to secure confidential treatment of such information as it would to protect its own confidential information from disclosure and shall be jointly and severally liable for any breach of this ARTICLE 14 by such Person.

14.4 **Terms of this Agreement.** The Parties acknowledge that this Agreement and all of the respective terms of this Agreement shall be treated as Confidential Information of both Parties.

14.5 **Publicity.** The Parties shall make a joint public announcement of the execution of this Agreement in the form attached as Exhibit 14.5, which shall be issued at a time to be mutually agreed by the Parties. Each Party agrees not to issue any other press release or other public statement disclosing other information relating to this Agreement or the transactions contemplated hereby that contains information not previously publicly disclosed in accordance with this Section 14.5 without the prior written consent of the other Party, not to be unreasonably withheld, conditioned or delayed.

14.6 **Securities Filings.** Notwithstanding anything to the contrary in this ARTICLE 14, in the event either Party proposes to file with the Securities and Exchange Commission or the securities regulators of any state or other jurisdiction a registration statement or any other disclosure document that describes or refers to the terms and conditions of this Agreement or any related agreements between the Parties, such Party shall notify the other Party of such intention and shall provide the other Party with a copy of relevant portions of the proposed filing at least ten (10) Business Days prior to such filing (and any revisions to such portions of the proposed filing a reasonable time prior to the filing thereof), including any exhibits thereto that refer to the other Party or the terms and conditions of this Agreement or any related agreements between the Parties. The Party making such filing shall cooperate in good faith with the other Party to obtain confidential treatment of the terms and conditions of this Agreement or any related agreements between the Parties that the other Party requests to be kept confidential or otherwise afforded confidential treatment, and shall only disclose Confidential Information that it is reasonably advised by outside counsel is legally required to be disclosed. No such notice and provision of a copy shall be required if the description of or reference to this Agreement or a related agreement

between the Parties contained in the proposed filing has been included in any previous filing made by the either Party in accordance with this Section 14.6 or otherwise approved by the other Party.

14.7 **Relationship to Confidentiality Agreement.** As of the Effective Date, this Agreement supersedes the Confidentiality Agreement; provided however, that all "Confidential Information" disclosed or received by the Parties thereunder shall be deemed Confidential Information hereunder and shall be subject to the terms and conditions of this Agreement.

14.8 **Equitable Relief.** Given the nature of the Confidential Information and the competitive damage that could result to a Party upon unauthorized disclosure, use or transfer of its Confidential Information to any Third Party, the Parties agree that monetary damages may not be a sufficient remedy for any breach of this ARTICLE 14. In addition to all other remedies, a Party shall be entitled to seek specific performance and injunctive and other equitable relief as a remedy for any breach or threatened breach of this ARTICLE 14.

14.9 **Publications.** All publications relating to the use of the Compound and/or a Product in the Licensed Field shall be prepared, presented and/or published in accordance with pharmaceutical industry accepted guidelines including: (a) International Committee of Medical Journal Editors (ICMJE) guidelines, (b) Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication, (c) Pharmaceutical Research and Manufacturers of America (PhRMA) guidelines, and (d) Principles on Conduct of Clinical Trials. Each Party will have the right to publish summaries of results of all Clinical Trials conducted by such Party with respect to the use of a Product in the Licensed Field after the Effective Date; *provided*, *however,* that the other Party will have the right to review and comment on all proposed publications prior to submission of such publication. The publishing Party shall provide the other Party at least sixty (60) days prior notice to review and comment on the Clinical Trials results, or non-clinical study results to be published for the purposes of preparing any necessary Patent filings.

14.10 **Clinical Trial Transparency**. Both Parties agree to collaborate to maintain compliance with all Applicable Laws related to clinical trial transparency, as well as any industry guidelines/codes of conduct, or other obligations that may apply to either the sponsor of any clinical trial and/or the owner of any Regulatory Approval, all as relates to any Research Product or Licensed Product. The Parties shall cooperate to maintain clinical trial transparency consistent with each sponsor's clinical trial registration, summary result, and data sharing transparency policies and will support disclosure of Information as needed based on the needs of the sponsors of the study or the Regulatory Approval holder with respect to any Research Product or Licensed Product.

ARTICLE 15 – TERM AND TERMINATION

15.1 **Term**. This Agreement shall become effective as of the Effective Date and shall continue in full force and effect, unless earlier terminated pursuant to this ARTICLE 15, until the later of the (a) expiration of the Collaboration Term, (b) the expiration of the Takeda Option Term, (c) the expiration of the Licensed Product Royalty Term with respect to all Licensed

Products in the Territory, or (d) the expiration of the Takeda Royalty Term with respect to all Products the Takeda Territory (the "Term").

15.2 **Termination for Material Breach**.

(a) Either Party (the "Non-breaching Party") may terminate this Agreement in its entirety (except as otherwise provided in this Section 15.2(a)) if the other Party (the "Breaching Party") has materially breached this Agreement, and such material breach has not been cured within sixty (60) days after receipt of written notice of such breach by the Breaching Party from the Non-Breaching Party (the "Cure Period"); provided, however, that, notwithstanding the foregoing, termination pursuant to this Section 15.2(a) shall be on a Compound-by-Compound and Product-by-Product basis unless such material breach materially diminishes, or materially frustrates, the value of this Agreement to the Non-breaching Party, taken as a whole, in which case the Non-breaching Party may terminate this Agreement in its entirety. Any termination of this Agreement with respect to a Compound or Product, or in its entirety, pursuant to this Section 15.2(a) shall become effective at the end of the Cure Period, unless the Breaching Party has cured any such material breach prior to the expiration of such Cure Period. The right of either Party to terminate this Agreement with respect to a Compound or Product, or in its entirety, as provided in this Section 15.2(a) shall not be affected in any way by such Party's waiver of or failure to take action with respect to any previous breach under this Agreement.

(b) If the Parties reasonably and in good faith disagree as to whether there has been a material breach, including whether such breach was material, the Party that disputes whether there has been a material breach may contest the allegation in accordance with ARTICLE 16. Notwithstanding anything to the contrary contained in Section 15.2(a), the Cure Period for any Dispute will run from the date that written notice was first provided to the Breaching Party by the Non-Breaching Party through the resolution of such Dispute pursuant to ARTICLE 16, and it is understood and acknowledged that, during the pendency of a Dispute pursuant to this Section 15.2(b), all of the terms and conditions of this Agreement shall remain in effect, and the Parties shall continue to perform all of their respective obligations under this Agreement.

(c) Notwithstanding the foregoing, following the execution of an Option Product License Agreement or Exercised Product License Agreement, the terms of such license agreement shall govern the handling of termination for material breach with respect to the activities that are the subject of such license agreement (which shall be on the basis of this Section 15.2) and any termination of this Agreement shall not affect the existence of such Option Product License Agreement or Exercised Product License Agreement.

15.3 **Termination for Safety Reasons.**

(a) Each Party shall have the right to terminate this Agreement on a Compound-by- Compound and Product-by-Product basis with respect to such Party's field and territory at any time upon providing ninety (90) days prior written notice to the other Party (i) if senior executives responsible for the terminating Party's pharmacovigilance and clinical science functions determine in good faith that the risk/benefit profile of the Compound or Product is such that the Compound or Product cannot continue to be Developed or administered to patients

safely; or (b) upon the occurrence of serious adverse events related to the use of the Compound or Product that cause the terminating Party to conclude that the continued use of the Compound or Product by patients will result in patients being exposed to a product in which the risks outweigh the benefits.

(b) Notwithstanding the foregoing, following the execution of an Option Product License Agreement or Exercised Product License Agreement, the terms of such license agreement shall govern the handling of termination for safety reasons with respect to the activities that are the subject of such license agreement (which shall be on the basis of this Section 15.3) and any termination of this Agreement shall not affect the existence of such Option Product License Agreement or Exercised Product License Agreement.

15.4 **Termination for Convenience**.

(a) Takeda shall have the right to terminate this Agreement with respect to the Takeda Option for any or no reason upon ninety (90) days written notice.

(b) Provided that Ultragenyx has completed Development activities for a Licensed [***] Product in the Takeda Field as set forth in the Initial [***] Development Plan pursuant to Section 4.3(a), after the end of the Collaboration Term Ultragenyx shall have the right to terminate this Agreement with respect to any or all Licensed Products in any or all countries for which it has rights with respect to such Licensed Products for any or no reason upon ninety (90) days written notice.

(c) Notwithstanding the foregoing, following the execution of an Option Product License Agreement or Exercised Product License Agreement, the terms of such license agreement shall govern the handling of termination for convenience with respect to the activities that are the subject of such license agreement (which shall be on the basis of this Section 15.4) and any termination of this Agreement shall not affect the existence of such Option Product License Agreement or Exercised Product License Agreement.

15.5 **Termination for Patent Challenge**.

(a) Takeda may terminate this Agreement with respect to the Licensed Products at any time upon providing written notice to Ultragenyx, if Ultragenyx, or any of Ultragenyx's Affiliates, directly, or indirectly through assistance granted to a Third Party, commences any interference or opposition proceeding, challenges the validity or enforceability of, or opposes any extension of or the grant of a supplementary protection certificate with respect to any Takeda Patent or any other Patent owned or controlled by Takeda that claims or discloses the composition of matter or the method of making or using a Licensed Product.

(b) Takeda may terminate this Agreement with respect to all Candidate Products and/or Option Products at any time upon providing written notice to Ultragenyx, if Ultragenyx, or any of Ultragenyx's Affiliates, directly, or indirectly through assistance granted to a Third Party, commences any interference or opposition proceeding, challenges the validity or enforceability of, or opposes any extension of or the grant of a supplementary protection

certificate with respect to any Takeda Patent or any other Patent Controlled by Takeda that claims or discloses the composition of matter or the method of making or using a Candidate Product and/or Option Product.

(c) Ultragenyx may terminate this Agreement with respect to an Ultragenyx Pipeline Product at any time upon providing written notice to Takeda, if Takeda, or any of Takeda's Affiliates, directly, or indirectly through assistance granted to a Third Party, commences any interference or opposition proceeding, challenges the validity or enforceability of, or opposes any extension of or the grant of a supplementary protection certificate with respect to any Ultragenyx Patent or any other Patent Controlled by Ultragenyx that claims or discloses the composition of matter or the method of making or using such Ultragenyx Pipeline Product.

(d) Notwithstanding the foregoing, following the execution of an Option Product License Agreement or Exercised Product License Agreement, the terms of such license agreement shall govern the handling of termination for patent challenge with respect to the activities that are the subject of such license agreement (which shall be on the basis of this Section 15.5) and any termination of this Agreement shall not affect the existence of such Option Product License Agreement or Exercised Product License Agreement.

15.6 **Termination for Insolvency**.

(a) Either Party may terminate this Agreement in its entirety upon providing written notice to the other Party on or after the time that such other Party makes a general assignment for the benefit of creditors, files an insolvency petition in bankruptcy, petitions for or acquiesces in the appointment of any receiver, trustee or similar officer to liquidate or conserve its business or any substantial part of its assets, commences under the laws of any jurisdiction any proceeding involving its insolvency, bankruptcy, reorganization, adjustment of debt, dissolution, liquidation or any other similar proceeding for the release of financially distressed debtors, or becomes a party to any proceeding or action of the type described above, and such proceeding or action remains un-dismissed or un-stayed for a period of more than ninety (90) days.

(b) All rights and licenses granted under or pursuant to this Agreement are, and shall otherwise be deemed to be, for purposes of Section 365(n) of Title 11 of the United States Code and other similar laws in any other jurisdiction outside of the Territory (collectively, the "Bankruptcy Laws"), licenses of rights to "intellectual property" as defined under the Bankruptcy Laws. If a case is commenced during the Term by or against a Party under Bankruptcy Laws then, unless and until this Agreement is rejected as provided pursuant to such Bankruptcy Laws, such Party (in any capacity, including debtor-in-possession) and its successors and assigns (including a Title 11 trustee) shall perform all of the obligations in this Agreement intended to be performed by such Party. If a case is commenced during the Term by or against a Party under the Bankruptcy Laws, this Agreement is rejected as provided for under the Bankruptcy Laws, and the non-bankrupt Party elects to retain its rights hereunder as provided for under the Bankruptcy Laws, then the Party subject to such case under the Bankruptcy Laws (in any capacity, including debtor-in-possession) and its successors and assigns (including a Title 11 trustee), shall provide to the non-bankrupt Party copies of all Patents and Information necessary for the non-bankrupt Party to prosecute, maintain and enjoy its rights under the terms of this

Agreement. All rights, powers and remedies of the non-bankrupt Party as provided herein are in addition to and not in substitution for any and all other rights, powers and remedies now or hereafter existing at law or in equity (including the Bankruptcy Laws) in the event of the commencement of a case by or against a Party under the Bankruptcy Laws. In particular, it is the intention and understanding of the Parties to this Agreement that the rights granted to the Parties under this Section 15.6 are essential to the Parties' respective businesses and the Parties acknowledge that damages are not an adequate remedy.

(c) Notwithstanding the foregoing, following the execution of an Option Product License Agreement or Exercised Product License Agreement, the terms of such license agreement shall govern the handling of termination for insolvency with respect to the activities that are the subject of such license agreement (which shall be on the basis of this Section 15.6) and any termination of this Agreement shall not affect the existence of such Option Product License Agreement or Exercised Product License Agreement.

15.7 **Effects of Termination**.

(a) **Effects of Termination of Agreement in its Entirety**

(i) In the event of a termination of this Agreement in its entirety by Ultragenyx pursuant to Section 15.2 (Breach) and 15.6 (Insolvency), Ultragenyx may elect either of the following options (A) or (B) by providing written notice of its election with its notice of termination:

(A) to effectuate actual termination of this Agreement in its entirety, in which case the following shall apply:

(I) all rights and licenses granted to Ultragenyx hereunder shall terminate immediately;

(II) all rights and licenses granted by Ultragenyx hereunder shall terminate immediately other than the Takeda [***] License, which license shall become non-exclusive under any intellectual property not assigned to Takeda pursuant to the remainder of this Section 15.7(a)(i)(A), and which license shall apply to the Licensed [***] Compound, Licensed Analog Compounds, Licensed Products and Research Products;

(III) Ultragenyx, as soon as reasonably practical after the effective date of such termination, shall provide to Takeda, as applicable and to the extent permitted under any applicable Third Party contract, (1) any Information, including copies of all Clinical Trial data and results, and the like developed by or for the benefit of Ultragenyx relating to a Licensed Product or Research Product, and (2) other documents to the extent relating to the Licensed [***] Compounds, Licensed Analog Compounds, [***] Compounds, Candidate Products, Licensed Products or Research Products that are necessary for their Exploitation. Ultragenyx will cooperate with Takeda to provide a transfer of such Information and documents at Takeda's expense. At Takeda's request, Ultragenyx shall assign to Takeda any and all agreements to which Ultragenyx, or its Affiliate, and a Third Party are parties, and that govern the Exploitation

activities conducted in connection with such Compounds or Products prior to such termination, or, if such assignment is not permitted under the relevant agreement: (i) grant to Takeda other rights to provide to Takeda the benefit of such non-assignable agreement, at Takeda's expense, to the extent permitted under the terms of such non-assignable agreement; or (ii) to the extent not permitted under the terms of such non-assignable agreement, the Parties shall discuss in good faith an alternative solution to enable Takeda to receive, at Takeda's expense, the benefit of the terms of such non-assignable agreement. In addition to the actions contemplated in this Section 15.7(a)(i)(A)(III), Ultragenyx shall take such other actions and execute such other instruments, assignments and documents, at Takeda's expense, as may be necessary to effect the transfer of rights to such Compound(s) and Product(s) hereunder to Takeda;

(IV) Ultragenyx shall, at Takeda's expense, transfer to Takeda any and all Regulatory Documentation related to a Licensed Product or Research Product, including any Product INDs and Product Regulatory Approvals and, upon Takeda's request, shall make available to Takeda any other relevant information reasonably related to such Regulatory Documentation; and

(V) effective on the date of termination, Ultragenyx, for itself and on behalf of its Affiliates, hereby assigns (and to the extent such assignment can only be made in the future hereby agrees to assign) to Takeda all right, title and interest in and to any Licensed Product Improvements, Licensed Product Improvement Patents, Option Product Improvements, and Option Product Improvement Patents, in each case where Controlled by Ultragenyx or its Affiliates. Ultragenyx will, at Takeda's expense, execute and record assignments and other necessary documents consistent with such change in ownership; or

(B) in lieu of actual termination under (A) above, Ultragenyx may elect that all rights and licenses granted to Ultragenyx hereunder shall continue under this Agreement and any milestone or royalty payments that become due to Takeda by Ultragenyx with respect to Licensed Product after such termination shall be [***] and paid to Takeda in accordance with the payment provisions of this Agreement. This Section 15.7(a)(i)(B) may only be exercised once.

(ii) In the event of a termination of this Agreement in its entirety by Takeda pursuant to Section 15.2 (Breach) or 15.6 (Insolvency), Takeda may elect either of the following options (A) or (B) by providing written notice of its election with its notice of termination:

(A) to effectuate actual termination of this Agreement in its entirety, in which case the following shall apply:

(I) all rights and licenses granted to Takeda hereunder shall terminate immediately, other than the Takeda [***] License, which license shall become non-exclusive under any intellectual property not assigned to Takeda pursuant to the remainder of this Section 15.7(a)(ii)(A), and which licenses shall apply to the Licensed [***] Compound, Licensed Analog Compounds, Licensed Products and Research Products;

(II) all rights and licenses granted by Takeda hereunder

shall terminate immediately;

(III) if not already completed and provided, Ultragenyx shall complete and provide a report of the Development activities for the Licensed [***] Product in the Takeda Field as set forth in the Initial [***] Development Plan in accordance with Section 4.3(a);

(IV) Ultragenyx, as soon as reasonably practical after the effective date of such termination, shall provide to Takeda, as applicable and to the extent permitted under any applicable Third Party contract, (1) any Information, including copies of all Clinical Trial data and results, and the like developed by or for the benefit of Ultragenyx relating to a Licensed Product or Research Product, and (2) other documents to the extent relating to the Licensed [***] Compounds, Licensed Analog Compounds, [***] Compounds, Candidate Products, Licensed Products or Research Products that are necessary for their Exploitation. Ultragenyx will cooperate with Takeda to provide a transfer of such material Information and documents at Ultragenyx's expense. At Takeda's request, Ultragenyx shall assign to Takeda any and all Patents and agreements to which Ultragenyx, or its Affiliate, and a Third Party are parties, and that govern the Exploitation activities conducted in connection with such Compounds or Products prior to such termination, or, if such assignment is not permitted under the relevant agreement: (i) grant to Takeda other rights to provide to Takeda the benefit of such non- assignable agreement, at Ultragenyx's expense, to the extent permitted under the terms of such non-assignable agreement; or (ii) to the extent not permitted under the terms of such non- assignable agreement, the Parties shall discuss in good faith an alternative solution to enable Takeda to receive, at Ultragenyx's expense, the benefit of the terms of such non-assignable agreement. In addition to the actions contemplated in this Section 15.7(a)(ii)(A)(IV), Ultragenyx shall take such other actions and execute such other instruments, assignments and documents, at Ultragenyx's expense, as may be necessary to effect the transfer of rights to such Compound(s) and Product(s) hereunder to Takeda;

(V) Ultragenyx shall, at its expense, transfer to Takeda any and all Regulatory Documentation related to a Licensed Product or Research Product, including any Product INDs and Product Regulatory Approvals and, upon Takeda's request, shall make available to Takeda any other relevant information reasonably related to such Regulatory Documentation; and

(VI) effective on the date of termination, Ultragenyx, for itself and on behalf of its Affiliates, hereby assigns (and to the extent such assignment can only be made in the future hereby agrees to assign) to Takeda all right, title and interest in and to any Licensed Product Improvements, Licensed Product Improvement Patents, Option Product Improvements, and Option Product Improvement Patents, in each case where Controlled by Ultragenyx or its Affiliates. Ultragenyx will, at its expense, execute and record assignments and other necessary documents consistent with such change in ownership; or

(B) in lieu of actual termination under (A) above, Takeda may elect that all rights and licenses granted to Takeda hereunder shall continue under this Agreement and any milestones or royalty payments that become due to Ultragenyx by Takeda with respect to

any Exercised Product after such termination shall be reduced by fifty percent (50%) and paid to Ultragenyx in accordance with the payment provisions of this Agreement. This Section 15.7(a)(ii)(B) may only be exercised once.

(iii) For clarity, an Exercised Product License Agreement or an Option Product License Agreement shall include termination provisions similar to this Section 15.7(a) and shall otherwise govern the effects of termination of such agreement in its entirety.

(b) **Effects of Termination of a Compound or Product for Safety Reasons.** In the event of a termination of this Agreement with respect to a particular Compound or Product pursuant to Section 15.3 (for the avoidance of doubt, not a Terminated Product) then:

(i) all license rights received by the terminating Party and all obligations of the terminating Party with respect to the terminated Compound or Product shall cease and, with respect to the terminating Party only, this Agreement shall automatically be deemed to be amended to exclude such rights and obligations of the terminating Party with respect to the terminated Compound or Product but shall otherwise survive and continue in effect for the remaining Compounds and Products; and

(ii) the non-terminating Party shall continue to have all rights and obligations under this Agreement with respect to the terminated Compound or Product (including the obligation to make royalty, milestone and other payments to the terminating Party) unless it also elects to terminate the particular Compound or Product pursuant to Section 15.3.

(c) **Effects of Termination with Respect to a Terminated Product.** In the event of termination of this Agreement with respect to a Terminated Product (but not in the case of any termination of this Agreement in its entirety) then:

(i) all rights and licenses granted hereunder by either Party shall automatically be deemed to be amended to exclude the Terminated Product but shall otherwise survive and continue in effect for the remaining Compounds and Products;

(ii) in the case of termination for convenience pursuant to Section 15.4, if an Option Negotiation Period or Takeda Option Negotiation Period is then ongoing, the Term with respect to such Option Product or Exercised Product, as applicable, will automatically extend until the earlier of (A) expiration of such Option Negotiation Period or Takeda Option Negotiation Period, as applicable, or (B) execution of the applicable Option Product License Agreement or Exercised Product License Agreement;

(iii) if the Terminated Product is a Licensed Product, if not already completed and provided, Ultragenyx shall complete and provide a report of the Development activities for the Licensed [***] Product in the Takeda Field as set forth in the Initial [***] Development Plan in accordance with Section 4.3(a);

(iv) Ultragenyx, as soon as reasonably practical after the effective date of such termination, shall provide to Takeda, as applicable and to the extent permitted under any

applicable Third Party contract, (A) any Information, including copies of all Clinical Trial data and results, and the like developed by or for the benefit of Ultragenyx relating to a Terminated Product, and (B) other documents to the extent relating to the Terminated Products that are necessary for their Exploitation. Ultragenyx will cooperate with Takeda to provide a transfer of such material Information and documents. Ultragenyx shall assign to Takeda any and all Patents and agreements to which Ultragenyx, or its Affiliate, and a Third Party are parties, and that govern the Exploitation activities conducted in connection with a Terminated Product prior to such termination, or, if such assignment is not permitted under the relevant agreement: (1) grant to Takeda other rights to provide to Takeda the benefit of such non-assignable agreement to the extent permitted under the terms of such non-assignable agreement; or (2) to the extent not permitted under the terms of such non-assignable agreement, the Parties shall discuss in good faith an alternative solution to enable Takeda to receive the benefit of the terms of such non- assignable agreement. In addition to the actions contemplated in this Section 15.7(c)(iv), Ultragenyx shall take such other actions and execute such other instruments, assignments and documents as may be necessary to effect the transfer of rights to such Terminated Products hereunder to Takeda. Each Party shall bear its own expenses under this Section 15.7(c)(iv);

(v) Ultragenyx shall transfer to Takeda any and all Regulatory Documentation directly and solely related to a Terminated Product, including any Product INDs and Product Regulatory Approvals and, upon Takeda's request, shall make available to Takeda any other relevant information reasonably related to such Regulatory Documentation;

(vi) effective on the date of termination, Ultragenyx, for itself and on behalf of its Affiliates, hereby assigns (and to the extent such assignment can only be made in the future hereby agrees to assign) to Takeda all right, title and interest in and to any Licensed Product Improvements, Licensed Product Improvement Patents, Option Product Improvements, and Option Product Improvement Patents to the extent the foregoing Cover a Terminated Product and are Controlled by Ultragenyx or its Affiliates. Ultragenyx will execute and record assignments and other necessary documents consistent with such change in ownership; and

(vii) Takeda shall have the right to assume all prosecution, maintenance, and enforcement activities with respect to Patents under this Agreement Covering the Terminated Products. Ultragenyx will cooperate with Takeda and provide Takeda with reasonable assistance and cooperation with the prosecution, maintenance, and enforcement activities with respect to such Patents.

(d) **Effect of Termination on Ultragenyx's Put Rights under the Common Stock Purchase Agreement**. Immediately upon (i) written notice of termination of this Agreement in its entirety pursuant to Section 15.2, or 15.6, (ii) written notice of termination of a Licensed Product or Research Product pursuant to Section 15.2, 15.3, 15.4, 15.5, 18.5 or (iii) upon the Ultragenyx [***] License terminating pursuant to Section 4.3(f), Ultragenyx's rights under the Common Stock Purchase Agreement to require the purchase of the Second Tranche Shares and Third Tranche Shares (as such terms are defined in the Common Stock Purchase Agreement) shall be suspended and such rights shall automatically terminate on the effective date of such termination, provided, however, there shall be no suspension or termination of such Ultragenyx

rights under the Common Stock Purchase Agreement to the extent Ultragenyx terminates the Agreement, a Licensed Product or Research Product pursuant to Section 15.2. Where written notice of termination pursuant to Section 15.2 is provided by Takeda, and Ultragenyx cures all material breaches during the Cure Period, the suspension shall be removed on the effective date of such cure.

15.8 **Effect of Expiration**

(a) **Expiration of Collaboration Term.** Upon expiration of the Collaboration Term for a given Research Product:

(i) All rights to such Research Product shall revert to Takeda except for those rights, if any, granted to Ultragenyx under an Option Product License Agreement;

(ii) As soon as reasonably practical after the effective date of expiration of the Collaboration Term for a given Research Product, Ultragenyx shall, except where otherwise provided under an Option Product License Agreement, provide to Takeda, as applicable and to the extent permitted under any applicable Third Party contract (1) any Information, including copies of all Clinical Trial data and results, and the like developed by or for the benefit of Ultragenyx relating to such Research Product and (2) other documents to the extent relating to such Research Product that are necessary for their continued Exploitation. Ultragenyx will cooperate with Takeda to provide a transfer of such material Information and documents. At Takeda's request, Ultragenyx shall assign to Takeda any and all Patents and agreements to which Ultragenyx, or its Affiliate, and a Third Party are parties, and that govern the Exploitation activities conducted in connection with such Research Product prior to such expiration, or if such assignment is not permitted under the relevant agreement: (i) grant to Takeda other rights to provide to Takeda the benefit of such non-assignable agreement to the extent permitted under the terms of such non-assignable agreement; or (ii) to the extent not permitted under the terms of such non-assignable agreement, the Parties shall discuss in good faith an alternative solution to enable Takeda to receive the benefit of the terms of such non-assignable agreement. In addition to the actions contemplated in this Section 15.8(a)(ii), Ultragenyx shall take such other actions and execute such other instruments, assignments and documents as may be necessary to effect the transfer of rights to such Product to Takeda. Each Party shall bear its own expenses under this Section 15.8(a)(ii);

(iii) Ultragenyx shall transfer to Takeda any and all Regulatory Documentation directly and solely related to such Research Product, including any Product INDs and Product Regulatory Approvals and, upon Takeda's request, shall make available to Takeda any other relevant information reasonably related to such Regulatory Documentation; and

(iv) Takeda shall have the right to assume all prosecution, maintenance, and enforcement activities with respect to Patents under this Agreement Covering such Research Product. Ultragenyx will cooperate with Takeda and provide Takeda with reasonable assistance and cooperation with the prosecution, maintenance, and enforcement activities with respect to such Patents.

(b) **Expiration of Licensed Product Royalty Term.** Upon the expiration of the Licensed Product Royalty Term for each Licensed Product in each country in the Territory, Ultragenyx shall have a non-exclusive, fully-paid up and irrevocable license under the Licensed [***] Technology with respect to such Licensed Product in such country in the Ultragenyx Field for Licensed Products.

(c) **Expiration of Exercised Product License Agreement and Option Product License Agreement**. Each Exercised Product License Agreement and Option Product License Agreement shall provide that, upon expiration of the applicable royalty term, Takeda shall have a non-exclusive, fully-paid up and irrevocable license with respect to the Exercised Products and Licensed Option Products, respectively.

15.9 **Remedies.** Notwithstanding anything to the contrary in this Agreement, except as otherwise set forth in this Agreement, termination or expiration of this Agreement shall not relieve the Parties of any liability or obligation which accrued hereunder prior to the effective date of such termination or expiration, nor prejudice either Party's right to obtain performance of any obligation. Each Party shall be free, pursuant to ARTICLE 16, to seek, without restriction as to the number of times it may seek, damages, costs and remedies that may be available to it under Applicable Laws or in equity and shall be entitled to offset the amount of any damages and costs obtained against the other Party in a final determination under Section 16.4, against any amounts otherwise due to such other Party under this Agreement.

15.10 **Survival**. The following provisions shall survive any expiration or termination of this Agreement for the period of time specified therein (or, if no such period is specified, indefinitely): ARTICLE 1 (Definitions); ARTICLE 16 (Dispute Resolution); and ARTICLE 17 (Indemnification); and Sections 4.5 (Records; Disclosure of Data and Results), 6.6(b) (Research Materials Transfer), 11.9, 11.10, 11.11, 11.12, 11.13 (Payment, Taxes, Audit); 12.1 (Ownership of Inventions); 14.1, 14.2, 14.3, 14.4, 14.5, 14.6, 14.7, 14.8 (Confidentiality); 15.7, 15.8, 15.9, 15.10 (Termination); 18.3, 18.7, 18.8, 18.9, 18.10, 18.14, 18.15, 18.16, and 18.17 (Miscellaneous).

ARTICLE 16 – DISPUTE RESOLUTION

16.1 **Exclusive Dispute Resolution Mechanism.** Except for disputes for which a Party has final decision making authority under this Agreement, including Sections 2.1(b)(ii), 2.2(c)(ii) and 12.4, the Parties agree that the procedures set forth in this ARTICLE 16 shall be the exclusive mechanism for resolving any dispute, controversy, or claim between the Parties that may arise from time to time pursuant to this Agreement relating to either Party's rights or obligations hereunder (each, a "Dispute", and collectively, the "Disputes") that is not resolved through good faith negotiation between the Parties.

16.2 **Resolution by Executive Officers.** In the event of any Dispute, the Parties shall first attempt in good faith to resolve such Dispute by negotiation and consultation between themselves. In the event that such Dispute is not resolved on an informal basis within ten (10) Business Days after receipt of writing notice of such Dispute by a Party, either Party may, by written notice to the other Party, refer the Dispute to the Senior Officers of the other Party for

attempted resolution by good faith negotiation within thirty (30) days after such notice is received. Except where exclusive decision-making authority rests with a Party under this Agreement (including Sections 2.1(b)(ii), 2.2(c)(ii) and 12.4), each Party may, in its sole discretion, seek resolution of any and all Disputes that are not resolved under this Section 16.2 using (a) arbitration pursuant Section 16.3 where arbitration pursuant to Section 16.3 is specifically provided for in this Agreement or (b) otherwise, pursuant to Section 16.4.

16.3 **Baseball Arbitration.** Any Dispute for which arbitration pursuant to this Section 16.3 is specifically provided for in this Agreement shall be finally decided by expedited arbitration in accordance with the following abbreviated dispute resolution procedures:

(a) If the Dispute is not resolved within thirty (30) days after referral to the Party's respective Senior Officers pursuant to Section 16.2, either Party may send the other Party a written notice that it wishes to resolve the Dispute by using a neutral Third Party who is an Expert with at least fifteen (15) years of experience in area of the Dispute (the "Neutral Expert"). The date of the other Party's receipt of such written notices shall be the "Notice Date."

(b) Within fifteen (15) Business Days of the Notice Date, each Party shall notify the other Party in writing of its appointed Expert (each, a "Representative Expert"). The Representative Experts for each Party shall jointly appoint the Neutral Expert within fifteen (15) Business Days.

(c) Within ten (10) Business Days after the appointment of the Neutral Expert, each Party shall submit to the other Party and the Neutral Expert a written summary regarding its position with respect to the Dispute. Contemporaneously with the submission of its written summary regarding its position, each Party shall provide the other Party and the Neutral Expert with copies of all documents it relied upon in its written summary; provided that each Party may redact any portion of such documents which are covered by an applicable privilege or do not relate to the subject matter of this Agreement. Within three (3) Business Days of receipt of the other Party's written summary regarding its position, each Party may submit an opposition statement of no more than five (5) pages in length (excluding exhibits and declarations). Neither Party will be allowed to conduct any discovery. Neither Party may have any communications (either written or oral) with the other Party's Representative Experts or the Neutral Expert other than for the sole purpose of engaging the expert panel or as expressly permitted in this Section 16.3; provided, that oral presentations and follow-up written submissions may be made to the Neutral Expert at such Neutral Expert's request. The Neutral Expert may consult in writing with the Representative Experts regarding the submissions made by either Party; provided that both Representative Experts are aware of such consultation and provided an opportunity to respond. Evaluating each Party's written submissions, the Neutral Expert shall, within ten (10) Business Days of receipt of the written opposition statement, select in total, either Takeda's submission or Ultragenyx's submission. Such decision shall be final, binding and not appealable.

(d) The Party whose submission is not selected shall be solely responsible for the expenses and fees of the Neutral Expert and the reasonable costs and fees of the other Party's Representative Expert.

16.4 **Litigation.** Any unresolved Dispute that was subject to Section 16.2, shall be brought exclusively in a court of competent jurisdiction, federal or state, located in New York, New York, and in no other jurisdiction. Each Party hereby consents to personal jurisdiction and venue in, and agrees to service of process issued or authorized by, such court.

16.5 **Preliminary Injunctions.** Notwithstanding anything in this Agreement to the contrary, a Party may seek a temporary restraining order or a preliminary injunction from any court of competent jurisdiction in order to prevent immediate and irreparable injury, loss, or damage on a provisional basis, pending the decision of the arbitrator(s) on the ultimate merits of any Dispute.

16.6 **Patent and Trademark Disputes.** Notwithstanding anything in this Agreement to the contrary, any and all issues regarding the scope, construction, validity, and enforceability of any Patent or trademark relating to a Product that is the subject of this Agreement shall be determined in a court or other tribunal, as the case may be, of competent jurisdiction under the applicable patent or trademark laws of the country in which such Patent or trademark rights were granted or arose.

16.7 **Confidentiality.** Any and all activities conducted under ARTICLE 16, including any and all proceedings and decisions under Section 16.4, shall be deemed Confidential Information of each of the Parties, and shall be subject to ARTICLE 14.

16.8 **WAIVER OF RIGHT TO JURY TRIAL**. In connection with the Parties' rights under Section 16.4, EACH PARTY, TO THE EXTENT PERMITTED BY APPLICABLE LAWS, KNOWINGLY, VOLUNTARILY, AND INTENTIONALLY WAIVES ITS RIGHT TO A TRIAL BY JURY IN ANY ACTION OR OTHER LEGAL PROCEEDING ARISING OUT OF OR RELATING TO THIS AGREEMENT AND THE TRANSACTIONS IT CONTEMPLATES. THIS WAIVER APPLIES TO ANY ACTION OR LEGAL PROCEEDING, WHETHER SOUNDING IN CONTRACT, TORT, OR OTHERWISE.

ARTICLE 17 – INDEMNIFICATION

17.1 **Indemnification by Ultragenyx.** Ultragenyx hereby agrees to defend, indemnify and hold harmless Takeda and its Affiliates, and each of their respective directors, officers, employees, agents and representatives (each, a "Takeda Indemnitee") from and against any and all claims, suits, actions, demands, liabilities, expenses and/or loss, including reasonable legal expense and attorneys' fees (collectively, the "Losses"), to which any Takeda Indemnitee may become subject as a result of any claim, demand, action or other proceeding by any Third Party (each, a "Claim") to the extent such Losses arise directly or indirectly out of: (i) the practice by Ultragenyx or its Affiliate of any license granted to it under ARTICLE 3; (ii) the Exploitation of a Compound or a Product by Ultragenyx, its Affiliates or its sublicensees on or after the Effective Date, including, for the avoidance of doubt, any Product Liabilities arising from the use of a Product in the Licensed Field in the Territory on or after the Effective Date and any Losses that may arise due to Ultragenyx, its Affiliates or its sublicensees continuing to Exploit a Compound or Product in its territory or field that is the subject matter of a termination by Takeda pursuant to Section 15.3; (iii) the Exploitation of any Ultragenyx Pipeline Product by Ultragenyx, its Affiliates or its licensees before the Effective Date, including, for the avoidance

of doubt, any Product Liabilities arising from the use of a Ultragenyx Pipeline Product; (iv) the breach by Ultragenyx of any warranty, representation, covenant or agreement made by Ultragenyx in this Agreement; (v) the negligence, gross negligence or willful misconduct (including to the extent such negligence, gross negligence or willful misconduct gives rise to Product Liabilities under any legal theory) of Ultragenyx, its Affiliate or its sublicensee, or any officer, director, employee, agent or representative thereof; except, with respect to each of subsections (i) through (v) above, to the extent such Losses arise directly or indirectly from the negligence, gross negligence or willful misconduct of any Takeda Indemnitee or the breach by Takeda of any warranty, representation, covenant or agreement made by Takeda in this Agreement. Notwithstanding the foregoing, following the execution of an Exercised Product License Agreement or Option Product License Agreement, the terms of such license agreement shall govern the indemnification terms with respect to such Product(s) that are the subject of such license agreement.

17.2 **Indemnification by Takeda.** Takeda hereby agrees to defend, indemnify and hold harmless Ultragenyx and its Affiliates and each of their respective directors, officers, employees, agents and representatives (each, an "Ultragenyx Indemnitee") from and against any and all Losses to which any Ultragenyx Indemnitee may become subject as a result of any Claim to the extent such Losses arise directly or indirectly out of: (i) the practice by Takeda or its Affiliate of any license granted to it under ARTICLE 3; (ii) the Exploitation of a Product by Takeda, its Affiliates or its sublicensees on or after the Effective Date, including, for the avoidance of doubt, any Product Liabilities arising from the use on or after the Effective Date of a Licensed [***] Product in the Takeda Field in the Territory and any Losses that may arise due to Takeda, its Affiliates or its sublicensees continuing to Exploit a Compound or Product in its territory or field that is the subject matter of a termination by Ultragenyx pursuant to Section 15.3; (iii) the Exploitation of any Licensed [***] Product, [***] Product or Candidate Product by Takeda, its Affiliates or its licensees before the Effective Date, including, for the avoidance of doubt, any Product Liabilities arising from the use of a Licensed [***] Product, [***] Product or Candidate Product by Takeda, its Affiliates or its licensees before the Effective Date, (iv) the breach by Takeda of any warranty, representation, covenant or agreement made by Takeda in this Agreement; (iv) the negligence, gross negligence or willful misconduct (including to the extent such negligence, gross negligence or willful misconduct gives rise to product liability Claims under any legal theory) of Takeda or its Affiliate or its licensee (other than Ultragenyx or its Affiliate or sublicensee), or any officer, director, employee, agent or representative thereof; except, with respect to each of subsections (i) through (iv) above, to the extent such Losses arise directly or indirectly from the negligence, gross negligence or willful misconduct of any Ultragenyx Indemnitee or the breach by Ultragenyx of any warranty, representation, covenant or agreement made by Ultragenyx in this Agreement. Notwithstanding the foregoing, following the execution of an Exercised Product License Agreement or Option Product License Agreement, the terms of such license agreement shall govern the indemnification terms with respect to such Product(s) that are the subject of such license agreement.

17.3 **Indemnification Procedures**.

(a) **Notice.** Promptly after a Takeda Indemnitee or an Ultragenyx Indemnitee (each, an "Indemnitee") receives notice of a pending or threatened Claim, such Indemnitee shall give written notice of the Claim to the Party from whom the Indemnitee is entitled to receive indemnification pursuant to Sections 17.1 or 17.2, as applicable (the "Indemnifying Party"). However, an Indemnitee's delay in providing or failure to provide such notice will not relieve the Indemnifying Party of its indemnification obligations, except to the extent it can demonstrate prejudice due to the delay or lack of notice.

(b) **Defense.** Upon receipt of notice under Section 17.3(a) from the Indemnitee, the Indemnifying Party will have the duty to either compromise or defend, at its own expense and by counsel (reasonably satisfactory to Indemnitee), such Claim. The Indemnifying Party will promptly (and in any event not more than twenty (20) days after receipt of the Indemnitee's original notice) notify the Indemnitee in writing that it acknowledges its obligation to indemnify the Indemnitee with respect to the Claim pursuant to this ARTICLE 17 and of its intention either to compromise or defend such Claim. Once the Indemnifying Party gives such notice to the Indemnitee, the Indemnifying Party is not liable to the Indemnitee for the fees of other counsel or any other expenses subsequently incurred by the Indemnitee in connection with such defense, other than the Indemnitee's reasonable costs of investigation and cooperation. However, the Indemnitee will have the right to employ separate counsel and to control the defense of a Claim at its own expense.

(c) **Cooperation.** The Indemnitee will cooperate fully with the Indemnifying Party and its legal representatives in the investigation and defense of any Claim. The Indemnifying Party will keep the Indemnitee informed on a reasonable and timely basis as to the status of such Claim (to the extent the Indemnitee is not participating in the defense of such Claim) and conduct the defense of such Claim in a prudent manner.

(d) **Settlement.** If an Indemnifying Party assumes the defense of a Claim, no compromise or settlement of such Claim may be effected by the Indemnifying Party without the Indemnitee's written consent (which consent will not be unreasonably withheld, conditioned or delayed), unless: (i) there is no finding or admission of any violation of law or any violation of the rights of any person and no effect on any other claims that may be made against the Indemnitee; (ii) the sole relief provided is monetary damages that are paid in full by the Indemnifying Party; and (iii) the Indemnitee's rights under this Agreement are not adversely affected. If the Indemnifying Party fails to assume defense of a Claim within a reasonable time, the Indemnitee may settle such Claim on such terms as it deems appropriate with the consent of the Indemnifying Party (which consent shall not be unreasonably withheld, conditioned or delayed), and the Indemnifying Party will be obligated to indemnify the Indemnitee for such settlement as provided in this ARTICLE 17.

17.4 **Insurance.** Each Party shall, at its own expense, procure and maintain during the Term and for a period of five (5) years thereafter, insurance policy/policies, including product liability insurance, adequate to cover its obligations hereunder and which are consistent with normal business practices of prudent companies similarly situated. Such insurance shall not be construed to create a limit of a Party's liability with respect to its indemnification obligations

under this ARTICLE 17. Each Party shall provide the other Party with written evidence of such insurance or self-insurance upon request. Each Party shall provide the other Party with prompt written notice of cancellation, non-renewal or material change in such insurance or self- insurance that could materially adversely affect the rights of such other Party hereunder, and shall provide such notice within thirty (30) days after any such cancellation, non-renewal or material change.

17.5 **Limitation of Liability.** EXCEPT FOR A PARTY'S OBLIGATIONS SET FORTH IN THIS ARTICLE 17, AND ANY BREACH OF ARTICLE 14 (CONFIDENTIALITY)**,** IN NO EVENT WILL EITHER PARTY BE LIABLE TO THE OTHER PARTY (OR THE OTHER PARTY'S AFFILIATES OR SUBLICENSEES) IN CONNECTION WITH THIS AGREEMENT FOR LOST REVENUE, LOST PROFITS, LOST SAVINGS, LOSS OF USE, DAMAGE TO GOODWILL, OR ANY CONSEQUENTIAL, INCIDENTAL, SPECIAL, EXEMPLARY, PUNITIVE OR INDIRECT DAMAGES UNDER ANY THEORY, INCLUDING CONTRACT, NEGLIGENCE, OR STRICT LIABILITY, EVEN IF THAT PARTY HAS BEEN PLACED ON NOTICE OF THE POSSIBILITY OF SUCH DAMAGES.

ARTICLE 18 – MISCELLANEOUS

18.1 HSR Act.

(a) Each of Ultragenyx and Takeda shall, within ten (10) Business Days after Execution Date, file with the United States Federal Trade Commission and the Antitrust Division of the United States Department of Justice, any HSR Filing required of it under the HSR Act with respect to the subject matter of this Agreement, which forms shall specifically request early termination of the initial HSR Act waiting period. The Parties will cooperate with one another to the extent necessary in the preparation of any such HSR Filing. The Parties hereto commit to instruct their respective counsel to cooperate with each other and use good faith, diligent efforts to facilitate and expedite the identification and resolution of any such issues and, consequently, the expiration of the applicable HSR Act waiting period, such good faith diligent efforts to include counsel's undertaking: (i) to keep each other appropriately informed of communications received from and submitted to personnel of the reviewing antitrust authority; and (ii) to confer with each other regarding appropriate contacts with and response to personnel of the United States Federal Trade Commission and the Antitrust Division of the United States Department of Justice. Each Party will be responsible for its own costs and expenses and Ultragenyx will be responsible for all filing fees associated with any HSR Filing. In respect of any HSR Filing, each of Ultragenyx and Takeda will use its good faith, diligent efforts to eliminate any concern on the part of any court or governmental authority regarding the legality of the proposed transaction, including cooperating in good faith with any government investigation and the prompt production of documents, information, and witnesses requested in the course of such of any such investigation, including those contained in a Request for Additional Information and Documentary Materials (as that term is defined in the HSR Act), and to cause the Effective Date of this Agreement to occur as soon as practical, as provided in Section 18.1(b). Nothing in this Section shall require either Party to consent to the divestiture or other disposition of any of its or its Affiliates' assets or to consent to any other structural or conduct remedy, and each Party and

its Affiliates shall have no obligation to contest, administratively or in court, any ruling, order or other action of the United States Federal Trade Commission and the Antitrust Division of the United States Department of Justice or any Third Party respecting the transactions contemplated by this Agreement.

(b) Except for the specific provisions expressly identified in Section 18.1(c), this Agreement shall not be effective until the (i) the HSR Conditions are met and (ii) the earlier of (A) the date on which the Tax Conditions are met, or (B) July 18, 2016, at which time this Agreement shall be effective automatically in its entirety (such date the "**Effective Date**").

(c) Notwithstanding Section 18.1(b) and anything in this Agreement to the contrary, the following provisions of this Agreement shall be in full force and effect as of the Execution Date: Sections 14.5 (Publicity) and 14.6 (Securities Filings), ARTICLE 1 (Definitions) and ARTICLE 18 (other than Sections 18.2, 18.5 and 18.6) (Miscellaneous).

(d) If the Effective Date has not occurred within one hundred eighty (180) days following the Execution Date, or such date as the Parties may mutually agree, this Agreement may be terminated by either Party on written notice to the other.

18.2 **Exports and Restrictions on Competition**.

(a) **Exports**. Except as provided in this Agreement, each Party shall not, and shall cause its Affiliates and sublicensees not to, whether directly or indirectly through a Third Party, export, distribute or sell:

(i) in the case of Ultragenyx, (A) Licensed [***] Products outside the Ultragenyx Field or outside the Territory, (B) Licensed Analog Products outside the Licensed Field or outside the Territory, (C) Research Products unless and until an Option Product License Agreement is executed for such Products and then only in accordance with such Option Product License Agreement; provided further that, if the Takeda Option has been exercised for a given Product Ultragenyx may not export, distribute or sell such Product in the Takeda Territory.

(ii) In the case of Takeda, Ultragenyx Pipeline Products outside of the Takeda Territory.

(b) [***] **Obligations**. Ultragenyx shall not, and shall cause its Affiliates not to, whether directly or indirectly through a Third Party (including any sublicensee), (i) [***] or (ii) [***]. Ultragenyx shall not be in breach of this Section 18.2(b) by acquiring, merging or consolidating with a Third Party which develops or commercializes [***]; provided, however, that in the event Ultragenyx acquires such [***], it must, unless Takeda agrees to the contrary, within [***] of such acquisition, either divest such [***] to a Third Party, [***], or, if applicable, terminate

this Agreement [***] in accordance with Section 15.4.

18.3 **Notice.** Any notice, request, or other communication permitted or required under this Agreement shall be in writing, shall refer specifically to this Agreement and shall be hand delivered or sent by a recognized overnight delivery service, costs prepaid, or by facsimile (with transmission confirmed), to the following addresses or to such other addresses as a Party may designate by written notice in accordance with this Section 18.3:

If to Takeda:

Takeda Pharmaceutical Company Limited 1-1, Doshomachi 4-
chome,
Chuo-ku, Osaka 540-8645
Attention: Head of Global Business Development Facsimile: (+81) 3-3278-2323

Copy to:

Takeda Pharmaceuticals U.S.A., Inc. One Takeda Parkway
Deerfield, IL 60015
Attention: General Counsel, Legal Department Facsimile: 224-554-7831

If to Ultragenyx:

Ultragenyx Pharmaceutical Inc. 60 Leveroni Court
Novato, CA 94949
Attention: Chief Business Officer

Copy to:

Cooley LLP
3175 Hanover Street Palo Alto,
CA 94304 Attention: Glen Sato
Fax: 650-849-7400

18.4 **Designation of Affiliates**. Each Party may discharge any obligations and exercise any rights hereunder through delegation of its obligations or rights to any of its Affiliates. Each Party hereby guarantees the performance by its Affiliates of such Party's obligations under this Agreement, and shall cause its Affiliates to comply with the provisions of this Agreement in connection with such performance. Any breach by a Party's Affiliate of any of such Party's obligations under this Agreement shall be deemed a breach by such Party, and the other Party

may proceed directly against such Party without any obligation to first proceed against such Party's Affiliate.

18.5 **Change of Control of Ultragenyx**.

(a) **Notice**. Ultragenyx (or its successor) shall provide notice to Takeda of any Change of Control of Ultragenyx within [***] Business Days after the date upon which the Ultragenyx Change of Control closes or otherwise becomes effective.

(b) **Effects of Change of Control of Ultragenyx**. In the event of a Change of Control of Ultragenyx, the following shall apply:

(i) The [***] applicable in the event of a Change of Control of Ultragenyx shall apply.

(ii) On or before the date that is [***] days after the date upon which a Change of Control of Ultragenyx closes or otherwise becomes effective, Takeda may take or require that Ultragenyx, or its successor, take or perform, as applicable, any one or more of the following actions: (A) Ultragenyx and its successor shall adopt [***], approved by [***], to prevent [***], (B) the [***] shall be [***] to be limited to those [***] as of the effective date of the Ultragenyx Change of Control, provided that if [***] has [***] shall be [***], (C) [***] shall be amended to require [***] written consent in order for [***] thereunder to the extent [***], and (D) [***] may [***], one or more of [***], in which case any [***] under [***] shall [***] and any [***] designated by [***] shall be deemed [***]; provided that to the extent that [***] in connection with the [***] on or before such date, such [***], as applicable, and associated [***] and such [***] shall not be deemed [***] under this Section 18.5(b)(ii). For clarity, [***] pursuant to this Section 18.5(b)(ii) shall not [***].

18.6 **Force Majeure.** Both Parties shall be excused from the performance of their obligations under this Agreement to the extent that such performance is prevented by Force Majeure and the nonperforming Party promptly provides notice of the prevention to the other Party. Such excuse shall be continued so long as the condition constituting Force Majeure continues and the nonperforming Party takes reasonable efforts to remove the condition. Notwithstanding the foregoing, a Party shall not be excused from making payments owed hereunder because of a Force Majeure affecting such Party. If a Force Majeure persists for more than ninety (90) days,

then the Parties will discuss in good faith the modification of the Parties' obligations under this Agreement in order to mitigate the delays caused by such Force Majeure.

18.7 **Assignment.** Prior to the Effective Date, neither Party may assign or transfer this Agreement or any rights or obligations hereunder without the prior written consent of the other. On or after the Effective Date, neither Party may assign or transfer this Agreement or any rights or obligations hereunder without the prior written consent of the other; provided that no such consent is required for (a) assignment to Affiliates or (b) in connection with the sale of all or substantially all of the assets to which this Agreement relates, whether in a merger, sale of stock, sale of assets or any other transaction (subject, in the case of Ultragenyx, to Section 18.5). Any successor or assignee of rights and/or obligations permitted hereunder shall, in writing to the other Party, expressly assume performance of such rights and/or obligations. Any permitted assignment shall be binding on the successors of the assigning Party. Any assignment or attempted assignment by either Party in violation of the terms of this Section shall be null, void and of no legal effect.

18.8 **Severability.** If any one or more of the provisions of this Agreement is held to be invalid or unenforceable by any court of competent jurisdiction from which no appeal can be or is taken, the provision shall be considered severed from this Agreement and shall not serve to invalidate any remaining provisions hereof. The Parties shall make a good faith effort to replace any invalid or unenforceable provision with a valid and enforceable one such that the objectives contemplated by the Parties when entering this Agreement may be realized.

18.9 **English Language.** This Agreement shall be written and executed in, and all other communications under or in connection with this Agreement, shall be in the English language. Any translation into any other language shall not be an official version thereof, and in the event of any conflict in interpretation between the English version and such translation, the English version shall control.

18.10 **Waiver and Non-Exclusion of Remedies.** Any term or condition of this Agreement may be waived at any time by the Party that is entitled to the benefit thereof, but no such waiver shall be effective unless set forth in a written instrument duly executed by or on behalf of the Party waiving such term or condition. The waiver by either Party hereto of any right hereunder or of the failure to perform or of a breach by the other Party shall not be deemed a waiver of any other right hereunder or of any other breach or failure by such other Party whether of a similar nature or otherwise. The rights and remedies provided herein are cumulative and do not exclude any other right or remedy provided by Applicable Laws or otherwise available except as expressly set forth herein.

18.11 **Further Assurance.** Each Party shall duly execute and deliver, or cause to be duly executed and delivered, such further instruments and do and cause to be done such further acts and things, including the filing of such assignments, agreements, documents, and instruments, as may be necessary or as the other Party may reasonably request in connection with this Agreement or to carry out more effectively the provisions and purposes hereof.

18.12 **Relationship of the Parties.** It is expressly agreed that Takeda, on the one hand, and Ultragenyx, on the other hand, shall be independent contractors and that the relationship between the two Parties shall not constitute a partnership, joint venture or agency. Neither Takeda nor Ultragenyx shall have the authority to make any statements, representations or commitments of any kind, or to take any action which shall be binding on the other, without the prior written consent of the other Party to do so. All persons employed by a Party shall be employees of that Party and not of the other Party and all costs and obligations incurred by reason of such employment shall be for the account and expense of such Party. For clarity, (a) if Takeda provides Research Support for an Ultragenyx Pipeline Product (other than Exercised Products) or Licensed Option Product (in connection with an Option Product License Agreement), Takeda shall be deemed an independent contractor in the performance of such Research Support and (b) in no case shall Takeda provide Research Support with respect to a Licensed Product.

18.13 **Counterparts.** This Agreement may be executed in two (2) or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. This Agreement may be executed by facsimile, .pdf or other electronically transmitted signatures and such signatures shall be deemed to bind each Party hereto as if they were the original signatures.

18.14 **Construction.** Except where the context otherwise requires, wherever used, the singular shall include the plural, the plural the singular, and the use of any gender shall be applicable to all genders. Whenever this Agreement refers to a number of days, such number refers to calendar days. The terms “including,” “include,” or “includes” as used herein shall mean “including, but not limited to,” and shall not limit the generality of any description preceding such term. The language of this Agreement shall be deemed to be the language mutually chosen by the Parties and no rule of strict construction shall be applied against either Party hereto. Each Party represents that it has been represented by legal counsel in connection with this Agreement and acknowledges that it has participated in the drafting hereof. In interpreting and applying the terms and provisions of this Agreement, the Parties agree that no presumption will apply against the Party which drafted such terms and provision.

18.15 **Governing Laws.** This Agreement was prepared in the English language, which language shall govern the interpretation of, and any dispute regarding, the terms of this Agreement. This Agreement and all disputes arising out of or related to this Agreement or any breach hereof shall be governed by and construed under the laws of the State of New York, without giving effect to any choice of law principles that would require the application of the laws of a different state.

18.16 **Entire Agreement.** This Agreement, including the Exhibits hereto, and the Common Stock Purchase Agreement set forth the complete, final and exclusive agreement and all the covenants, promises, agreements, warranties, representations, conditions and understandings between the Parties hereto with respect to the subject matter hereof and supersedes, as of the Execution Date, all prior and contemporaneous agreements and understandings between the Parties with respect to the subject matter hereof; provided, that, until the Effective Date, the Confidentiality Agreement shall continue in full force and effect in accordance with its terms.

Except as provided in the Common Stock Purchase Agreement, there are no covenants, promises, agreements, warranties, representations, conditions or understandings, either oral or written, between the Parties other than as are set forth herein and therein. No subsequent alteration, amendment, change or addition to this Agreement shall be binding upon the Parties unless reduced to writing and signed by an authorized officer of each Party. In the event of any inconsistency between the body of this Agreement and the Exhibits to this Agreement, the Common Stock Purchase Agreement, or any subsequent agreements ancillary to this Agreement, unless otherwise expressly stated to the contrary in such Exhibit, Common Stock Purchase Agreement or subsequent ancillary agreement, the terms contained in this Agreement shall control.

18.17 **Headings.** The headings of each Article and Section in this Agreement have been inserted for convenience of reference only and are not intended to limit or expand on the meaning of the language contained in the particular Article or Section.

SIGNATURE PAGE FOLLOWS

THIS AGREEMENT is executed by the authorized representatives of the Parties as of the Execution Date.

ULTRAGENYX PHARMACEUTICAL INC.	**TAKEDA PHARMACEUTICALCOMPANY LIMITED**
By /s/ Emil Kakkis	By /s/ Misako Hamamura
Name: Emil Kakkis	Name: Misako Hamamura
Title: CEO	Title: Head of JP Strategy & BD

Exhibit 1.6(i)

[***]

Chemical Name: [***]

Molecular Formula: [***]
Molecular Weight: [***]

Exhibit 1.6(iii)

[***]

CONFIDENTIAL TREATMENT REQUESTED

Certain information in this document has been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment has been requested with respect to omitted portions marked "***".

Exhibit 1.82

Initial [***] **Development Plan**

Initial Development Plan Framework

[***]

Estimated Timeline

[***]

Development Activities and Budget

[***]

Exhibit 1.91 Knowledge Group

Ultragenyx Position Titles

Tom Kassberg, SVP and Chief Business Officer Shalini Sharp, SVP and Chief Financial Officer Sunil Agarwal, SVP and Chief Medical Officer Cori Leonard, VP, Regulatory
Yael Weiss, Executive Director, Search and Evaluation, Business Development Rob Anstey, Senior Director, Business Development

Takeda Position Titles

[***]

Exhibit 1.94

[***]

- Chemical Name: [***]
- Molecular Formula: [***]
- Molecular Weight: [***]

Exhibit 1.99

Licensed Analog Compounds

[***]

CONFIDENTIAL TREATMENT REQUESTED

Certain information in this document has been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment has been requested with respect to omitted portions marked "***".

Exhibit 1.137 Preexisting Third Party IP

[***]

CONFIDENTIAL TREATMENT REQUESTED

Certain information in this document has been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment has been requested with respect to omitted portions marked "***".

Exhibit 1.141 Product INDs

[***]

CONFIDENTIAL TREATMENT REQUESTED

Certain information in this document has been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment has been requested with respect to omitted portions marked "***".

Exhibit 1.168
Takeda Patents

Licensed [***] **Patent**

Patent / Publication	**Priority / *Application***	**Inventor(s) / Assignee(s)**	**Title / Claims**	**Status**
[***]	[***]	[***]	[***]	[***]

Exhibit 1.188
Ultragenyx
Patents

Ultragenyx [***] **Patents**

[***]

Ultragenyx [***] Patents

[***]

Exhibit 1.195

[***]

CONFIDENTIAL TREATMENT REQUESTED

Certain information in this document has been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment has been requested with respect to omitted portions marked "***".

Exhibit 6.1 Listed Compounds

[***]

Exhibit 6.3(a)

[***] **Research Plan**

[***]

Exhibit 6.10(b)

[***]

Exhibit 13.2(b)

[***]

CONFIDENTIAL TREATMENT REQUESTED
Certain information in this document has been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment has been requested with respect to omitted portions marked "***".

Exhibit 14.5
Form of Press Release

Contact Ultragenyx Pharmaceutical Inc. Investors & Media
Ryan Martins 844-758-7273

For Takeda Pharmaceutical Company Limited: Tsuyoshi Tada – Japan
tsuyoshi.tada@takeda.com
+81332782417

Julia Ellwanger – USA julia.ellwanger@takeda.com
+1-224-554-7681

Ultragenyx and Takeda enter into a Collaboration to Develop and Commercialize Therapies for Rare Genetic Diseases

Ultragenyx to license and develop one or more product candidates from Takeda Takeda to make equity investment in Ultragenyx to fund development

NOVATO, CA, June 7, 2016 and OSAKA, JAPAN, June 8, 2016 – Ultragenyx Pharmaceutical Inc. (NASDAQ: RARE), a biopharmaceutical company focused on the development of novel products for rare and ultra- rare genetic diseases, and Takeda Pharmaceutical Company Limited (TSE: 4502), today announced a strategic partnership to develop and commercialize therapies to treat rare genetic diseases.

Ultragenyx will initially receive an exclusive license to one preclinical Takeda product candidate in a pre- determined field of use, and will have an exclusive option to co-develop and co-commercialize the product candidate in additional therapeutic areas. The companies have also established a five-year research collaboration in which Ultragenyx will have the option to license up to five additional Takeda

product candidates for rare diseases after the parties agree on and conduct initial validation activities under the purview of a Joint Research Committee.

“This broad collaboration provides Ultragenyx with a product opportunity that is approaching clinical- stage development as well as a potential continued source of new product candidates that will help us achieve our goal of bringing a new therapy into the clinic every one to two years,” said Emil D. Kakkis, MD, PhD, Chief Executive Officer of Ultragenyx. “Takeda has an impressive early pipeline of therapies with potential across a number of rare genetic diseases, and we are pleased that Takeda has chosen to partner with us to bring these therapies to patients with rare diseases that have few or no treatment options.”

"Ultragenyx is a rapidly emerging rare disease company, led by a highly experienced and successful management team," said Andrew Plump, M.D., Ph.D., Chief Medical and Scientific Officer of Takeda. “This partnership provides Takeda access to Ultragenyx’s strong patient-centric development and regulatory capabilities in the rare disease space, and could create significant value for both companies by delivering important new therapies to patients.”

Takeda will receive an exclusive option to commercialize any licensed products resulting from the collaboration in Asia, including Japan. In addition, Takeda receives an option to exclusively license one Ultragenyx pipeline product in Japan. Each company will receive potential development and sales milestone payments and royalties on net sales of licensed products by the other party.

Takeda will invest up to $65 million in Ultragenyx in two tranches, the first of which will comprise a $25million stock purchase along with a $15 million cash premium at closing. This will be followed at Ultragenyx’s option, within 12 months, by a second equity purchase of $25million with no additional premium. A potential third equity investment by Takeda is contingent upon Ultragenyx achieving a specific development milestone on a second asset. No additional financial details were disclosed.

The completion of the transactions are subject to Hart-Scott-Rodino Antitrust Improvements Act of 1976 (HSR) review and the satisfaction of other customary closing conditions.

About Ultragenyx

Ultragenyx is a clinical-stage biopharmaceutical company committed to bringing to market novel products for the treatment of rare and ultra-rare diseases, with a focus on serious, debilitating genetic diseases. Founded in 2010, the company has rapidly built a diverse portfolio of product candidates with the potential to address diseases for which the unmet medical need is high, the biology for treatment is clear, and for which there are no approved therapies.

The company is led by a management team experienced in the development and commercialization of rare disease therapeutics. Ultragenyx’s strategy is predicated upon time and cost-efficient drug development, with the goal of delivering safe and effective therapies to patients with the utmost urgency.

For more information on Ultragenyx, please visit the company's website at www.ultragenyx.com.

About Takeda

Takeda Pharmaceutical Company Limited (TSE: 4502) is a global, R&D-driven pharmaceutical company committed to bringing better health and a brighter future to patients by translating science into life- changing medicines. Takeda focuses its research efforts on oncology, gastroenterology and central nervous system therapeutic areas. It also has specific development programs in specialty cardiovascular diseases as well as late-stage candidates for vaccines. Takeda conducts R&D both internally and with partners to stay at the leading edge of innovation. New innovative products, especially in oncology, central nervous system and gastroenterology, as well as its presence in emerging markets, fuel the growth of Takeda. More than 30,000 Takeda employees are committed to improving quality of life for patients, working with our partners in health care in more than 70 countries. For more information, visit http://www.takeda.com/news.

Ultragenyx Forward-Looking Statements

Except for the historical information contained herein, the matters set forth in this press release, including statements regarding the potential to develop the licensed product candidate in additional therapeutic areas, as well as the potential to develop additional rare disease targets pursuant to the collaboration and the ability to bring new therapies to clinic, are forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. Such forward-looking statements involve substantial risks and uncertainties that could cause our development programs, future results, performance or achievements to differ significantly from those expressed or implied by the forward-looking statements. Such risks and uncertainties include, among others, the satisfaction of the HSR requirements and the impact on the timing of the closing, whether any products will be successfully developed and commercialized from the collaboration, uncertainties inherent in the drug development process and other matters that could affect the potential for success of the collaboration, including the sufficiency of existing cash, cash equivalents and short-term investments to fund operations. Ultragenyx undertakes no obligation to update or revise any forward-looking statements. For a further description of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to the business of the company in general, see Ultragenyx's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on March 10 2016, and its subsequent periodic reports filed with the Securities and Exchange Commission.

Takeda Forward-Looking Statements

This press release contains "forward-looking statements." Forward-looking statements include all statements other than statements of historical fact, including plans, strategies and expectations for the future, statements regarding the expected timing of filings and approvals relating to the transaction, the expected timing of the completion of the transaction, the ability to complete the transaction or to satisfy the various closing conditions, future revenues and profitability from or

growth or any assumptions underlying any of the foregoing. Statements made in the future tense, and words such as "anticipate," "expect," "project," "continue," "believe," "plan," "estimate," "pro forma," "intend," "potential," "target," "forecast," "guidance," "outlook," "seek," "assume," "will," "may," "should," and similar expressions are intended to qualify as forward-looking statements. Forward-looking statements are based on estimates and assumptions made by management that are believed to be reasonable, though they are inherently uncertain and difficult to predict. Investors and security holders are cautioned not to place undue reliance on these forward-looking statements.

Forward-looking statements involve risks and uncertainties that could cause actual results or experience to differ materially from that expressed or implied by the forward-looking statements. Some of these risks and uncertainties include, but are not limited to: required regulatory approvals for the transaction may not be obtained in a timely manner, if at all; the conditions to closing of the transaction may not be satisfied; competitive pressures and developments; applicable laws and regulations; the success or failure of product development programs; actions of regulatory authorities and the timing thereof; changes in exchange rates; and claims or concerns regarding the safety or efficacy of marketed products or product candidates in development.

The forward-looking statements contained in this press release speak only as of the date of this press release, and neither Ultragenyx nor Takeda undertakes any obligation to revise or update any forward-looking statements to reflect new information, future events or circumstances after the date of the forward-looking statement. If one or more of these statements is updated or corrected, investors and others should not conclude that additional updates or corrections will be made.

Exhibit 10.3

Ultragenyx Pharmaceutical

April 26, 2016

Karah Parschauer

Re: Offer of Employment

Dear Karah,

On behalf of Ultragenyx Pharmaceutical Inc. (the "Company"), I am pleased to present to you an offer of full-time employment as Executive Vice President and General Counsel. The Company's Board of Directors (the "Board") and I are excited about the important contributions you can make by joining the Ultragenyx management team and are confident that you will play a key role in our company's growth and success. In your role as General Counsel (GC), you will report directly to me and be a member of the Executive Leadership Team, or XLT. In the GC role, you will act as a strategic partner and business advisor to the CDO, the XLT and the Board of Directors as well as provide the technical and leadership experience to run the Company's legal function. You will provide guidance and advice on critical legal, business and compliance matters facing the organization through the transition to becoming a global commercial business, working with all functions of Ultragenyx as the company focuses on the commercialization of its pipeline. As an XLT member, you will have a role in setting the strategic direction of the company along with the other XLT members, as well as contributing to decisions that might affect other departments directly as well as the execution of the company's plans.

You will lead and develop a growing legal and compliance department and devising a legal strategy to help the Company reach its business goals. You will oversee directly corporate general and clinical trial contract activities, SEC-related legal activities, the compliance function for non-GXP issues, intellectual property, and legal support for business development. You will be responsible for the establishment of appropriate compliance systems in preparation for anticipated drug launches building on the existing Compliance Committee. As for all functions at Ultragenyx, the Legal group is expected to work in an integrated fashion with commercial, development, program management, technical operations, and business development to drive the growth and success of the company. This includes establishing, maintaining and evolving the critical and unique strategies for development at Ultragenyx which depend on close collaborations between departments, and novel approaches to traditional clinical development challenges. This includes working with the CFO and CCO on global commercial business planning, the CFO and CBO on corporate defense and any M&A activities, the CBO and CEO on intellectual property issues and the CMO on clinical trial startup activities.

Compensation

In the regular exempt position of General Counsel, the Company shall pay you as compensation for your services an initial base salary at a gross annual rate of $350,000 (the "Base Salary"). Such Base Salary shall be payable in accordance with the Company's standard payroll procedures and subject to standard payroll deductions and withholdings. The Board or the Compensation Committee of the Board shall review your Base Salary at least annually.

In addition to your Base Salary, pursuant to the Company's corporate bonus plan (or such other incentive plan maintained by the Company) you will be eligible to earn an annual bonus of up to 40% of your Base Salary based upon your performance during the previous year as evaluated by the CEO in consultation with the Board (or Compensation Committee of the Board) against pre-determined individual and/or corporate performance goals. In addition, the Company will provide you with a sign-on bonus in the amount of $50,000, subject to applicable federal and state taxes, to be paid within 30 days of your start date. In the event that you should voluntarily terminate your employment with Ultragenyx, or are terminated for "cause", within twelve (12) months of your hire date, you shall, no later than the effective date of such termination, refund to the Company the full amount of such bonus payment

paid by the Company. The Employee further agrees to pay all costs reasonably incurred by Ultragenyx in connection with the collection of such refund, including reasonable attorney's fees.

Equity Grants

Subject to the approval of the Compensation Committee, you will receive an option to purchase up to an aggregate of 60,000 shares of the Company's Common Stock (the "Option") pursuant to the Company's 2014 Incentive Plan (the "Plan"). The exercise price of the Option will be equal to the closing price per share of Common Stock on the date of grant.

The Option will vest and become exercisable as follows: 1/4th of the shares initially subject to the Option shall vest and become exercisable on the first (1st) anniversary of the first day of your employment with the Company, and thereafter 1/48th of the shares initially subject to the Option shall vest and become exercisable each month until the Option is fully vested, in each case subject to your continued employment by the Company (or its subsidiaries). The Option shall be governed by the Company's standard form of stock option agreements and the Plan.

Subject to the approval of the Compensation Committee, you will also receive a grant of 7,500 restricted stock units (the "RSUs") pursuant to the Plan. The RSUs will vest annually over a four-year period from the date of grant (i.e., 25% of the RSUs shall vest and become exercisable on each anniversary of the date of grant during the four-year period), in each case subject to your continued employment by the Company (or its consolidated subsidiaries). The RSUs shall be governed by the Company's standard form of restricted stock unit agreement and the Plan.

Notwithstanding the foregoing, in the event that (i) the Company consummates a Covered Transaction (as defined in the Plan), (ii) on the date such Covered Transaction is consummated you are employed by the Company (or its subsidiaries) and (iii) within 12 months after the date such Covered Transaction is consummated your employment by the Company (or its successor or subsidiaries) is terminated without Cause (as defined below) or you resign such employment due to a Constructive Termination (as defined below), then provided such termination constitutes a "separation from service" (as defined under Treasury Regulation Section 1.409A-1(h), without regard to any alternative definition thereunder, a "Separation from Service"), in addition to the severance benefits set forth below, the vesting of any equity-based compensation awards granted to you in connection with your employment shall accelerate with respect to 100% of the then-unvested shares then subject to such awards.

Relocation

The Company will provide you with assistance in the amount up to $50,000, for the relocation of your current primary residence to the Bay Area. The amount provided is intended to cover expenses including household goods move and any other incidentals related to your move. An estimate of the costs will be provided to the Company for final approval. In addition, the Company will provide up to six (6) months of temporary housing at the Company's partnered facility. You will be responsible for any taxable expenses related to relocation subject to standard IRS guidelines. In the event that you should voluntarily terminate your employment with Ultragenyx, or are terminated for "cause", within twelve (12) months after date of relocation of your personal residence, you shall, no later than the effective date of such termination, refund to the Company the full amount of such relocation benefits paid by the Company. The Employee further agrees to pay all costs reasonably incurred by Ultragenyx in connection with the collection of such refund, including reasonable attorney's fees.

Benefits

You will be eligible to participate in all of the employee benefits and benefit plans that the Company generally makes available to its full-time regular employees, subject to the terms and conditions of such benefits and benefit plans. At this time, these will include at a minimum, medical, dental and vision insurance coverage. Coverage for these benefits begins on the 1st day of the month following your date of hire. Detailed information about the benefits presently available will be provided to you on your first day of employment.

The health plan options will include 4 medical plans (2-HMO, PPO and HSA), a dental and vision plan, life/AD&D insurance, disability and voluntary insurance as well as a 401(k) retirement plan, with a company match of 3%. The

Company will cover 90% of the employee benefit costs and 75% of the dependent benefits costs. Based on conditions and situations over time, the Company may change specific benefits and plans from time to time, but our intent is to provide an excellent health benefit program to our employees.

You will accrue vacation time at the rate of four weeks (160 hours) per year, up to an accrual cap of 240 hours, under the terms of the Company's PTO policy. You will also be eligible for 5 sick days.

"At Will" Employment

Employment with the Company is "at-will". This means that it is not for any specified period of time and can be terminated by you or by the Company at any time, with or without advance notice, and for any or no particular reason or Cause. It also means that your job duties, title, responsibilities, reporting level, compensation and benefits, as well as the Company's personnel policies and procedures, may be changed at any time, with or without notice in the sole discretion of the Company. This "at-will" nature of your employment shall remain unchanged during your tenure as an employee, and can only be changed by an express written agreement that is signed by you and by the Company's CEO.

Severance

If, at any time, your employment with the Company or its successor is terminated without Cause, or you resign your employment due to a Constructive Termination, then provided such termination constitutes a Separation from Service, the Company shall: (i) extend the exercise period applicable to the Option (and to any other options to purchase the Company's Common Stock you then hold) such that you will have until the date that is twelve (12) months after the date of your Separation from Service to exercise any of the vested shares (determined as of the date of your Separation from Service) subject to the Option (but in no event will the exercise period be extended until later than the date of expiration of the term of the Option as set forth in the agreement evidencing such Option); and (ii) the Company shall pay you, as severance, the equivalent of one (1) year of your Base Salary in effect as of the date of your Separation from Service, subject to standard payroll deductions and withholdings (the "Severance Amount"). The Severance Amount will be paid in installments in the form of continuation of your Base Salary payments, paid on the Company's regular payroll dates, commencing on the Company's first regular payroll date that follows the 60th day after such Separation from Service. The first regular payroll date that follows the 60th day after such Separation from Service shall be for all accrued Base Salary for the 60-day period plus the period from the 60th day until the regular payroll date; the remainder of the Base Salary continuation payments shall thereafter be made on the Company's regular payroll dates.

Notwithstanding anything herein to the contrary, the receipt of any of the severance or acceleration benefits described in this letter will be subject to and conditioned upon: (i) your signing a separation agreement and release of claims in a form reasonably satisfactory to the Company (the "Separation Agreement") and such Separation Agreement becoming effective and irrevocable as specified therein no later than sixty (60) days following your Separation from Service; and (ii) your continued compliance with the terms of this letter, the Separation Agreement, the enclosed Confidential Information and Invention Assignment Agreement (including without limitation, your not using or disclosing any confidential or proprietary information of the Company), and any other agreement entered into between you and the Company. No severance benefits of any kind will be paid or provided, and no acceleration of vesting shall be effective, until the Separation Agreement becomes effective. You shall also resign from all positions and terminate any relationships as an employee, advisor, officer or director with the Company and any of its affiliates, each effective on the date of termination.

Additionally, and for the avoidance of doubt, in the event that the Company terminates your employment for Cause, or you resign your employment for any reason other than due to a Constructive Termination, or your employment terminates upon your death or disability, you will no longer vest in the Option or the RSUs (or any other equity) and you will not be entitled to any severance benefits described herein.

For purposes of this offer letter, "Cause" means any of the following: (i) your gross negligence in carrying out, or material failure to carry out, your duties for the Company (including without limitation, your failure to cooperate in any Company investigation), after notice from the Board and a reasonable opportunity to cure (if deemed curable); (ii) any breach of your fiduciary duties to the Company, after notice from the Board and a reasonable opportunity to

cure (if deemed curable); (iii) conviction of, or plea of guilty or no contest to, any felony; (iv) any act of fraud or embezzlement by you with respect to your obligations or otherwise relating to the business of the Company; (v) your material violation of any Company policy; (vi) your material breach of any agreement entered into between you and the Company; or (vii) your unauthorized use or disclosure of confidential information or trade secrets of the Company or its affiliates.

For the purposes of this letter, "Constructive Termination" means the occurrence of any of the following events without your written consent: (i) a material reduction or change in your job duties, responsibilities and requirements from your job duties, responsibilities and requirements immediately prior to such reduction or change, taking into account the differences in job title and duties that are normally occasioned by reason of an acquisition of one company by another; (ii) a material reduction of your Base Salary (other than an equal, across-the-board reduction in the compensation of all similarly-situated employees of the Company or the surviving entity that is approved by the Board); or (iii) a requirement that you relocate to a principal office that increases your one-way commute by more than 50 miles relative to your immediately preceding principal office. Notwithstanding the foregoing, none of the foregoing events or conditions will constitute Constructive Termination unless: (x) you provide the Company with written objection (or notice) to the event or condition within 30 days following the occurrence thereof, (y) the Company does not reverse or otherwise cure the event or condition within 30 days of receiving that written objection, and (z) you resign your employment within 30 days following the expiration of that cure period.

Notwithstanding any other provision herein or any other plan, arrangement or agreement to the contrary, if any of the payments or benefits provided or to be provided by the Company or its affiliates to you or for your benefit pursuant to the terms of this Offer Letter or otherwise ("Covered Payments") constitute parachute payments ("Parachute Payments") within the meaning of Section 280G of the Internal Revenue Code of 1986, as amended (the "Code") and would, but for this paragraph be subject to the excise tax imposed under Section 4999 of the Code (or any successor provision thereto) or any similar tax imposed by state or local law or any interest or penalties with respect to such taxes (collectively, the "Excise Tax"), then the Covered Payments shall be either (i) reduced to the minimum extent necessary to ensure that no portion of the Covered Payments is subject to the Excise Tax (that amount, the "Reduced Amount") or (ii) payable in full if your receipt on an after-tax basis of the full amount of payments and benefits (after taking into account the applicable federal, state, local and foreign income, employment and excise taxes (including the Excise Tax)) would result in you receiving an amount greater than the Reduced Amount.

Any reduction pursuant to the preceding paragraph shall be made in a manner consistent with the requirements of Section 409A of the Code and the following: (i) the Covered Payments which do not constitute nonqualified deferred compensation subject to Section 409A of the Code shall be reduced first; and (ii) all other Covered Payments shall then be reduced as follows: (A) cash payments shall be reduced before non-cash payments; and (B) payments to be made on a later payment date shall be reduced before payments to be made on an earlier payment date.

Any such required determination shall be made in writing in good faith by an independent accounting firm selected by the Company (the "Accountants"), which shall provide detailed supporting calculations to the Company and you as reasonably requested by the Company or you. The Company and you shall provide the Accountants with such information and documents as the Accountants may reasonably request in order to make a determination. For purposes of making the calculations and determinations required herein, the Accountants may rely on reasonable, good faith assumptions and approximations concerning the application of Section 280G and Section 4999 of the Code. The Accountants' determinations shall be final and binding on the Company and you. The Company shall be responsible for all fees and expenses incurred by the Accountants in connection with the calculations required herein.

Compliance with Section 409A

It is intended that all of the severance benefits and other payments payable under this letter satisfy, to the greatest extent possible, the exemptions from the application of Code Section 409A provided under Treasury Regulations 1.409A-1(b)(4), 1.409A-1(b)(5) and 1.409A-1(b)(9), and this letter agreement will be construed to the greatest extent possible as consistent with those provisions, and to the extent not so exempt, this letter (and any definitions

hereunder) will be construed in a manner that complies with Section 409A. Any payment by the Company under this letter agreement that is subject to Section 409A and that is contingent on a termination of employment is contingent on a "separation from service" within the meaning of Section 409A. Each such payment shall be considered to be a separate payment for purposes of Section 409A. Notwithstanding any provision to the contrary in this letter, if you are deemed by the Company at the time of your Separation from Service to be a "specified employee" for purposes of Code Section 409A(a)(2)(B)(i), and if any of the payments upon Separation from Service set forth herein and/or under any other agreement with the Company are deemed to be "deferred compensation", then to the extent delayed commencement of any portion of such payments is required in order to avoid a prohibited distribution under Code Section 409A(a)(2)(B)(i) and the related adverse taxation under Section 409A, such payments shall not be provided to you prior to the earliest of (i) the expiration of the six-month period measured from the date of your Separation from Service with the Company, (ii) the date of your death, or (iii) such earlier date as permitted under Section 409A without the imposition of adverse taxation. Upon the first business day following the expiration of such applicable Code Section 409A(a)(2)(B)(i) period, all payments deferred pursuant to this paragraph shall be paid in a lump sum to you, and any remaining payments due shall be paid as otherwise provided herein or in the applicable agreement. No interest shall be due on any amounts so deferred.

Compliance with Company Policies

As an employee of the Company, you will be expected to comply with the Company's personnel and other policies, including but not limited to, the Company's policies prohibiting discrimination and unlawful harassment, conflicts of interest and violation of applicable laws in the course of performing services to the Company. During your orientation, you will be provided with the Company's policy and procedures.

Full-time Services to the Company

The Company requires that, as a full-time employee, you devote your full business time, attention, skills and efforts to the tasks and duties of your position as assigned by the Company. However, the Company will not preclude you from providing services to others, so long as such services would not be to the benefit of a competitor of the Company and will not otherwise interfere with your ability to satisfactorily fulfill your job responsibilities to the Company. If you wish to perform services (for any or no form of compensation) to any other person or business entity while employed by the Company, please contact the CEO and discuss your plans in advance of providing such services so that no problem later arises that could have been avoided from the outset. Any other such services must be approved by the CEO and Board.

Conditions

This offer, and any employment pursuant to this offer, is conditioned upon the following:

- Your ability to provide satisfactory documentary proof of your identity and right to work in the United States of America on your first day of employment. Enclosed is the INS Form I-9, Employment Eligibility Verification, the second page of which includes a description of acceptable documentary proof.
- Your signed agreement to, and ongoing compliance with, the terms of the enclosed Confidential Information and Invention Assignment Agreement without modification.
- Your consent (by your signature below) to, and results satisfactory to the Company of, reference and background checks. Until you have been informed in writing by the Company that such checks have been completed and the results satisfactory to the Company, you should defer reliance on this offer.
- Your return to me of the enclosed copy of this letter, after being signed by you without modification.

No Conflicting Obligations

By signing and accepting this offer, you represent and warrant that: (i) you are not subject to any pre-existing contractual or other legal obligation with any person, company or business enterprise which may be an impediment to or is inconsistent with your employment with, or your providing services to, the Company; (ii) you have not and shall not bring onto Company premises, or use or disclose in the course of your employment with the Company, any

confidential or proprietary information or trade secrets of another person, company or business enterprise; (iii) you have returned all property and confidential information belonging to any prior employer; and (iv) you are not relying on any representations, promises or agreements not expressly contained in this letter.

Choice of Law and Severability

This letter shall be interpreted in accordance with the laws of the State of California without giving effect to provisions governing the choice of law. If any provision of this letter becomes or is deemed invalid, illegal or unenforceable in any applicable jurisdiction by reason of the scope, extent or duration of its coverage, then such provision shall be deemed amended to the minimum extent necessary to conform to applicable law so as to be valid and enforceable or, if such provision cannot be so amended without materially altering the intention of the parties, then such provision shall be stricken and the remainder of this letter shall continue in full force and effect. If any provision of this letter is rendered illegal by any present or future statute, law, ordinance or regulation (collectively, the "Law") then that provision shall be curtailed or limited only to the minimum extent necessary to bring the provision into compliance with the Law. All the other terms and provisions of this letter shall continue in full force and effect without impairment or limitation.

Entire Agreement

If you accept this offer, and the conditions of this offer are satisfied, this letter and the written agreements referenced in this letter shall constitute the complete agreement between you and the Company with respect to the initial terms and conditions of your employment. Any representations, promises or agreements, whether written or oral, not contained in this letter or contrary to those contained in this letter, that may have been made to you are expressly cancelled and replaced by this offer letter. Except as otherwise specified in this letter or in the written agreements referenced in this letter, the terms and conditions of your employment pursuant to this letter may not be changed, except by a writing issued by the CEO with approval by the Board.

We look forward to you accepting this offer and a mutually rewarding relationship. As with all important decisions, you should make a decision concerning this offer based on your own investigation and judgment concerning the Company and its prospects, independent of the opinions and perspectives that may have been shared with you by any Company employee.

Please date and sign below, on the enclosed copy of this letter and return it to me no later than May 1, 2016. Once the offer has been accepted, we would like you to start on or before June 27, 2016. Please retain the original of this letter for your records. You should bring your INS Form I-9 required identification and proof of authorization to work with you on your first day of employment.

We look forward to working with you on developing treatment for many rare genetic diseases and hope you find your employment at Ultragenyx Pharmaceutical a rewarding experience. If you have any questions regarding this offer letter, please feel free to contact me at (415) 483-8800.

Warm Regards,

/s/ Emil Kakkis

Emil D. Kakkis, M.D., Ph.D.
Chief Executive Officer

I accept the above offer:

Signature: /s/ Karah Parschauer Dated: April 28, 2016

Print Name: Karah Parschauer

Exhibit 31.1

CERTIFICATION PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Emil D. Kakkis, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Ultragenyx Pharmaceutical Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of registrant's Board of Directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Dated: August 8, 2016

/s/ Emil D Kakkis
Emil D. Kakkis, M.D., Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Shalini Sharp, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Ultragenyx Pharmaceutical Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of registrant's Board of Directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Dated: August 8, 2016

/s/ Shalini Sharp
Shalini Sharp
Chief Financial Officer and Executive Vice President
(Principal Financial Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002 (18 U.S.C. SECTION 1350)

In connection with the accompanying Quarterly Report of Ultragenyx Pharmaceutical Inc. (the "Company") on Form 10-Q for the quarter ended June 30, 2016 (the "Report"), I, Emil D. Kakkis, M.D., Ph.D., as President and Chief Executive Officer of the Company, and Shalini Sharp, as Chief Financial Officer and Executive Vice President of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: August 8, 2016

/s/ Emil D. Kakkis
Emil D. Kakkis, M.D., Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Dated: August 8, 2016

/s/ Shalini Sharp
Shalini Sharp
Chief Financial Officer and Executive Vice President
(Principal Financial Officer)