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, 2019

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)

Not Applicable
(Former Name, Former Address and Former Fiscal Year, if Changed Since Last Report)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol	Name of each exchange on which registered
Common Stock, $0.001 par value	**RARE**	**The Nasdaq Global Select Market**

As of July 26, 2019, the registrant had 57,691,957 shares of common stock issued and outstanding.

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 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 ☑ NO ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted 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 such files). YES ☑ NO ☐

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

Large accelerated filer	☑	Accelerated filer	☐
Non-accelerated filer	☐	Smaller reporting company	☐
		Emerging growth company	☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

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

ULTRAGENYX PHARMACEUTICAL INC.

FORM 10-Q FOR THE QUARTER ENDED JUNE 30, 2019

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q (the Quarterly Report) 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 are forward-looking statements. In some cases, you can identify forward-looking statements by words such as “anticipate,” “believe,” “contemplate,” “continue,” “could,” “estimate,” “expect,” “forecast,” “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 commercialization, marketing, and manufacturing capabilities and strategy;
- our expectations regarding the timing of clinical study commencements and reporting results from same;
- the timing and likelihood of regulatory approvals for our product candidates;
- the anticipated indications for our product candidates, if approved;
- the potential market opportunities for commercializing our products and product candidates;
- our expectations regarding the potential market size and the size of the patient populations for our products and product candidates, if approved for commercial use;
- estimates of our expenses, 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, products and product candidates and the integration and performance of any businesses we have acquired or may acquire;
- the initiation, timing, progress, and results of ongoing and future preclinical 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 products and product candidates;
- our ability to maintain and establish collaborations or strategic relationships or obtain additional funding;
- our ability to maintain and establish relationships with third parties, such as contract research organizations, contract manufacturing organizations, suppliers, and distributors;
- our financial performance and the expansion of our organization;
- our ability to obtain supply of our products and product candidates;
- the scalability and commercial viability of our manufacturing methods and processes;
- 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 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. 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 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 amounts)

	June 30, 2019	December 31, 2018
Assets		
Current assets:		
Cash and cash equivalents	$ 131,337	$ 113,432
Short-term investments	486,949	346,274
Accounts receivable	20,901	12,740
Inventory	13,632	7,065
Prepaid expenses and other current assets	46,612	42,858
Total current assets	699,431	522,369
Property and equipment, net	25,317	20,046
Investment in Arcturus equity securities	24,167	—
Intangible assets, net	129,069	129,223
Goodwill	44,406	44,406
Right-of-use assets	33,356	—
Other assets	3,181	3,514
Total assets	$ 958,927	$ 719,558
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 8,743	$ 12,275
Accrued liabilities	59,264	62,450
Short-term lease liabilities	6,999	—
Total current liabilities	75,006	74,725
Deferred tax liabilities	31,166	31,166
Long-term lease liabilities	32,968	—
Other liabilities	—	4,759
Total liabilities	139,140	110,650
Stockholders' equity:		
Preferred stock — 25,000,000 shares authorized; nil outstanding as of June 30, 2019 and December 31, 2018	—	—
Common stock — 250,000,000 shares authorized; 57,665,375 and 50,860,588 shares issued and outstanding as of June 30, 2019 and December 31, 2018, respectively	58	51
Additional paid-in capital	2,045,685	1,639,773
Accumulated other comprehensive income (loss)	255	(633)
Accumulated deficit	(1,226,211)	(1,030,283)
Total stockholders' equity	819,787	608,908
Total liabilities and stockholders' equity	$ 958,927	$ 719,558

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,	
	2019	2018	2019	2018
Revenues:				
Collaboration and license	$ 19,247	$ 10,519	$ 33,485	$ 19,881
Product sales	4,902	2,275	8,836	3,590
Total revenues	24,149	12,794	42,321	23,471
Operating expenses:				
Cost of sales	766	141	1,218	366
Research and development	96,045	76,835	174,150	152,339
Selling, general and administrative	39,812	30,718	78,641	62,153
Total operating expenses	136,623	107,694	254,009	214,858
Loss from operations	(112,474)	(94,900)	(211,688)	(191,387)
Interest income	4,063	2,448	7,149	4,185
Gain from sale of priority review vouchers	—	40,322	—	170,322
Change in fair value of investment in Arcturus equity securities	9,828	—	9,828	—
Other expense	(376)	(496)	(788)	(5,454)
Loss before income taxes	(98,959)	(52,626)	(195,499)	(22,334)
Provision for income taxes	(213)	(102)	(429)	(141)
Net loss	$ (99,172)	$ (52,728)	$ (195,928)	$ (22,475)
Net loss per share, basic and diluted	$ (1.72)	$ (1.06)	$ (3.54)	$ (0.46)
Shares used in computing net loss per share, basic and diluted	57,519,308	49,819,528	55,376,336	49,046,838

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,	
	2019	2018	2019	2018
Net loss	$ (99,172)	$ (52,728)	$ (195,928)	$ (22,475)
Other comprehensive income (loss):				
Foreign currency translation adjustments	26	225	155	(64)
Transfer of cumulative translation adjustment for the substantial liquidation of foreign subsidiaries	—	—	—	5,272
Unrealized gain (loss) on available-for-sale securities	377	67	733	(182)
Other comprehensive income:	403	292	888	5,026
Total comprehensive loss	$ (98,769)	$ (52,436)	$ (195,040)	$ (17,449)

See accompanying notes.

ULTRAGENYX PHARMACEUTICAL INC.
CONDENSED CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
(Unaudited)
(In thousands, except share amounts)

	Common Stock		Additional Paid-In	Accumulated Other Comprehensive	Accumulated	Total Stockholders'
	Shares	Amount	Capital	Income (Loss)	Deficit	Equity
Balance as of March 31, 2019	57,303,888	$ 57	$ 2,013,859	$ (148)	$ (1,127,039)	$ 886,729
Issuance of common stock in connection with at-the-market offering, net of issuance costs	88,978	—	5,523	—	—	5,523
Employee stock-based compensation	—	—	22,490	—	—	22,490
Issuance of common stock under equity plan awards, net of tax	272,509	1	3,813	—	—	3,814
Other comprehensive income	—	—	—	403	—	403
Net loss	—	—	—	—	(99,172)	(99,172)
Balance as of June 30, 2019	57,665,375	$ 58	$ 2,045,685	$ 255	$ (1,226,211)	$ 819,787

	Common Stock		Additional Paid-In	Accumulated Other Comprehensive	Accumulated	Total Stockholders'
	Shares	Amount	Capital	Income (Loss)	Deficit	Equity
Balance as of December 31, 2018	50,860,588	$ 51	$ 1,639,773	$ (633)	$ (1,030,283)	$ 608,908
Issuance of common stock in connection with underwritten public offering, net of issuance costs	5,833,333	6	330,409	—	—	330,415
Issuance of common stock in connection with at-the-market offering, net of issuance costs	468,685	—	24,828	—	—	24,828
Employee stock-based compensation	—	—	42,960	—	—	42,960
Issuance of common stock under equity plan awards, net of tax	502,769	1	7,715	—	—	7,716
Other comprehensive income	—	—	—	888	—	888
Net loss	—	—	—	—	(195,928)	(195,928)
Balance as of June 30, 2019	57,665,375	$ 58	$ 2,045,685	$ 255	$ (1,226,211)	$ 819,787

	Common Stock		Additional Paid-In	Accumulated Other Comprehensive	Accumulated	Total Stockholders'
	Shares	Amount	Capital	Income (Loss)	Deficit	Equity
Balance as of March 31, 2018	49,665,203	$ 50	$ 1,526,972	$ (946)	$ (802,419)	$ 723,657
Employee stock-based compensation	—	—	19,563	—	—	19,563
Issuance of common stock under equity plan awards, net of tax	450,853	—	13,187	—	—	13,187
Other comprehensive income	—	—	—	292	—	292
Net loss	—	—	—	—	(52,728)	(52,728)
Balance as of June 30, 2018	50,116,056	$ 50	$ 1,559,722	$ (654)	$ (855,147)	$ 703,971

	Common Stock		Additional Paid-In	Accumulated Other Comprehensive	Accumulated	Total Stockholders'
	Shares	Amount	Capital	Income (Loss)	Deficit	Equity
Balance as of December 31, 2017	44,167,071	$ 44	$ 1,221,762	$ (5,680)	$ (832,672)	$ 383,454
Issuance of common stock in connection with underwritten public offering, net of issuance costs	5,043,860	5	270,964	—	—	270,969
Issuance of common stock in connection with at-the-market offering, net of issuance costs	240,417	1	11,807	—	—	11,808
Employee stock-based compensation	—	—	38,360	—	—	38,360
Issuance of common stock under equity plan awards, net of tax	664,708	—	16,829	—	—	16,829
Other comprehensive income	—	—	—	5,026	—	5,026
Net loss	—	—	—	—	(22,475)	(22,475)
Balance as of June 30, 2018	50,116,056	$ 50	$ 1,559,722	$ (654)	$ (855,147)	$ 703,971

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

	Six Months Ended June 30,	
	2019	**2018**
Operating activities:		
Net loss	$ (195,928)	$ (22,475)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation	42,428	38,360
Amortization of discount on investment securities, net	(2,960)	(913)
Depreciation and amortization	4,225	12,240
Foreign currency remeasurement loss	567	5,846
Change in fair value of investment in Arcturus equity securities	(9,828)	—
Gain from sale of priority review vouchers	—	(170,322)
Other	(132)	(145)
Changes in operating assets and liabilities:		
Accounts receivable	(8,161)	(12,253)
Inventory	(6,040)	(2,585)
Prepaid expenses and other current assets	(4,265)	(7,544)
Right-of-use assets	(17,200)	—
Other assets	1,010	(102)
Accounts payable	(3,644)	1,376
Lease liabilities	18,522	—
Accrued liabilities and other liabilities	(3,432)	(7,039)
Net cash used in operating activities	(184,838)	(165,556)
Investing activities:		
Purchase of property and equipment	(8,299)	(1,852)
Purchase of investments	(461,088)	(408,683)
Purchase of investment in Arcturus equity securities	(14,339)	—
Proceeds from the sale of investments	22,600	4,954
Proceeds from maturities of investments	301,507	112,162
Proceeds from sale of priority review vouchers	—	170,322
Net cash used in investing activities	(159,619)	(123,097)
Financing activities:		
Proceeds from the issuance of common stock in connection with underwritten public offerings, net	330,415	270,969
Proceeds from the issuance of common stock in connection with at-the-market offering, net	24,828	11,789
Proceeds from the issuance of common stock from equity plan awards, net of tax	7,716	16,829
Net cash provided by financing activities	362,959	299,587
Effect of exchange rate changes on cash	(30)	(647)
Net increase in cash, cash equivalents and restricted cash	18,472	10,287
Cash, cash equivalents and restricted cash at beginning of period	115,525	103,041
Cash, cash equivalents and restricted cash at end of period	$ 133,997	$ 113,328
Supplemental disclosures of non-cash information:		
Acquired lease liabilities arising from obtaining right-of-use assets	$ 21,515	$ —

See accompanying notes.

1. Organization

Ultragenyx Pharmaceutical Inc. (the Company) is a biopharmaceutical company 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 serious rare and ultra-rare genetic diseases. The Company has two approved therapies. Crysvita® (burosumab) is approved in the United States by the U.S. Food and Drug Administration (FDA) and in Canada for the treatment of X-linked hypophosphatemia (XLH) in adult and pediatric patients one year of age and older, and has received European conditional marketing authorization for the treatment of XLH with radiographic evidence of bone disease in children one year of age and older and adolescents with growing skeletons. In Brazil, Crysvita is approved for treatment of XLH in adult and pediatric patients one year of age and older. The Company has also received FDA approval for Mepsevii™ (vestronidase alfa), the first medicine approved for the treatment of children and adults with mucopolysaccharidosis VII (MPS VII), also known as Sly syndrome. In the European Union, Mepsevii is approved under exceptional circumstances for patients of all ages for the treatment of non-neurological manifestations of MPS VII. In Brazil, Mepsevii is approved for the treatment of MPS VII for patients of all ages.

In addition to the approved treatments for XLH and MPS VII, the Company has four ongoing clinical development programs. Crysvita is being studied for the treatment of tumor induced osteomalacia (TIO), a rare disease that impairs bone mineralization. UX007 is being studied 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. The Company has two gene therapy pipeline candidates: DTX301 is an adeno-associated virus 8 (AAV8) gene therapy product candidate in development for the treatment of patients with ornithine transcarbamylase (OTC) deficiency, the most common urea cycle disorder; and DTX401 is an AAV8 gene therapy product candidate for the treatment of patients with glycogen storage disease type Ia (GSDIa). The Company operates as one reportable segment.

The Company has sustained operating losses and expects such annual losses to continue over the next several years. The Company's ultimate success depends on the outcome of its research and development and commercialization activities, for which it expects to incur additional losses in the future. Management recognizes the need to raise additional capital to fully implement its business plan. Through June 30, 2019, the Company has relied primarily on the proceeds from equity offerings to finance its operations.

The Company intends to raise additional capital through the issuance of equity, borrowings, or strategic alliances with partner companies. However, if such financing is not available at adequate levels, the Company will need to reevaluate its operating plans.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying unaudited condensed consolidated financial statements include the accounts of the Company and its 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 19, 2019 with the United States Securities and Exchange Commission (SEC).

The results of operations for the three and six months ended June 30, 2019 are not necessarily indicative of the results to be expected for the year ending December 31, 2019. The condensed consolidated balance sheet as of December 31, 2018 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 accompanying consolidated financial statements have been prepared in accordance with GAAP. The preparation of the 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 consolidated financial statements and the accompanying notes. On an ongoing basis, management evaluates its estimates, including those related to clinical trial accruals, fair value of assets and liabilities, income taxes, and stock-based compensation. 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.

Cash, Cash Equivalents and Restricted Cash

Restricted cash primarily consists of money market accounts as collateral for the Company's obligations under its facility leases. The following table provides a reconciliation of cash, cash equivalents, and restricted cash reported within the consolidated balance sheets that sum to the total of the same such amounts shown in the consolidated statement of cash flows (in thousands):

	June 30,	
	2019	2018
Cash and cash equivalents	$ 131,337	$ 110,854
Restricted cash included in prepaid expenses and other current assets	161	652
Restricted cash included in other assets	2,499	1,822
Total cash, cash equivalents, and restricted cash shown in the statements of cash flows	$ 133,997	$ 113,328

Investment in Equity Securities

In June 2019, the Company entered into an amendment to the Research Collaboration and License Agreement and an Equity Purchase Agreement with Arcturus Therapeutics Holdings Inc. ("Arcturus"). Pursuant to the Equity Purchase Agreement, the Company purchased 2,400,000 shares of common stock, or approximately 18.2% of Arcturus's outstanding shares of common stock as of the closing date of the transaction and received an option to purchase an additional 600,000 shares of common stock. The investment was accounted for using the equity method of accounting as it was determined that the Company has significant influence over, but does not control the significant activities of Arcturus. The Company elected to apply the fair value option to account for the equity investment in Arcturus. The decision to elect the fair value option is irrevocable and is determined on an instrument by instrument basis. The option to purchase additional stock was accounted for at fair value using Black-Scholes option pricing method. The changes in fair value of the equity investment and option to purchase additional stock are included in the Condensed Consolidated Statements of Operations. See "Note 6. License and Research Agreements" for additional details on the Arcturus transaction.

Revenue Recognition

Collaboration and license revenue

The Company has certain license and collaboration agreements that are within the scope of Accounting Standards Codification (ASC) 808, *Collaborative Agreements*, which provides guidance on the presentation and disclosure of collaborative arrangements. Generally, the classification of the transactions under the collaborative arrangements is determined based on the nature of contractual terms of the arrangement, along with the nature of the operations of the participants. The Company records its share of collaboration revenue, net of transfer pricing related to net sales in the period in which such sales occur, if the Company is considered as an agent in the arrangement. The Company is considered an agent when the collaboration partner controls the product before transfer to the customers and has the ability to direct the use of and obtain substantially all of the remaining benefits from the product. Funding received related to research and development services and commercialization costs is generally classified as a reduction of research and development expenses and selling, general and administrative expenses, respectively, in the consolidated statement of operations, because the provision of such services for collaborative partners are not considered to be part of the Company's ongoing major or central operations.

The Company also receives royalty revenues under certain of the Company's license or collaboration agreements in exchange for license of intellectual property. If the Company does not have any future performance obligations for these license or collaboration agreements, royalty revenue is recorded as the underlying sales occur.

In order to record collaboration revenue, the Company utilizes certain information from its collaboration partners, including revenue from the sale of the product, associated reserves on revenue, and costs incurred for development and sales activities. For the periods covered in the financial statements presented, there have been no material changes to prior period estimates of revenues and expenses.

The terms of the Company's collaboration agreements may contain multiple performance obligations, which may include licenses and research and development activities. The Company evaluates these agreements under ASC 606, *Revenue from Contracts with Customers* (ASC 606), to determine the distinct performance obligations. The Company analogizes to ASC 606 for the accounting for distinct performance obligations for which there is a customer relationship. Prior to recognizing revenue, the Company makes estimates of the transaction price, including variable consideration that is subject to a constraint. Amounts of variable consideration are included in the transaction price to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur and when the uncertainty associated with the variable consideration is subsequently resolved. Total consideration may include nonrefundable upfront license fees, payments for research and development activities, reimbursement of certain third-party costs, payments based upon the achievement of specified milestones, and royalty payments based on product sales derived from the collaboration.

If there are multiple distinct performance obligations, the Company allocates the transaction price to each distinct performance obligation based on its relative standalone selling price. The standalone selling price is generally determined based on the prices charged to customers or using expected cost plus margin. The Company estimates the efforts needed to complete the performance obligation and recognizes revenue by measuring the progress towards complete satisfaction of the performance obligation using an input measure.

Product sales

The Company sells its approved products through a limited number of distributors. Under ASC 606, revenue from product sales is recognized at the point in time when the delivery is made and when title and risk of loss transfers to these distributors. The Company also recognizes revenue from sales of certain products on a "named patient" basis, which are allowed in certain countries prior to the commercial approval of the product. Prior to recognizing revenue, the Company makes estimates of the transaction price, including any variable consideration that is subject to a constraint. Amounts of variable consideration are included in the transaction price to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur and when the uncertainty associated with the variable consideration is subsequently resolved. Product sales are recorded net of estimated government-mandated rebates and chargebacks, estimated product returns, and other deductions.

Provisions for returns and other adjustments are provided for in the period the related revenue is recorded, as estimated by management. These reserves are based on estimates of the amounts earned or to be claimed on the related sales and are reviewed periodically and adjusted as necessary. If actual results vary, the Company may need to adjust these estimates, which could have an effect on earnings in the period of the adjustment.

Leases

The Company adopted Accounting Standards Update (ASU) No. 2016-02, *Leases (Topic 842)* as of January 1, 2019 using the modified retrospective method. The results for the three and six months ended June 30, 2019 are presented under ASC 842. The results for the three and six months ended June 30, 2018 and other prior period amounts were not adjusted and continue to be reported in accordance with historical accounting under prior lease guidance, ASC 840, *Leases (Topic 840)*. The Company also elected the package of practical expedients under the transition guidance that will retain the historical lease classification and initial direct costs for any leases that existed prior to adoption of the new guidance and the practical expedient to not separate lease and non-lease components.

The Company determines if an arrangement includes a lease at inception. Right-of-use assets and lease liabilities are recognized based on the present value of the future minimum lease payments over the lease term at the commencement date. The right-of-use asset includes any lease payments made and excludes lease incentives. Incremental borrowing rate is used in determining the present value of future payments. The Company applies a portfolio approach to the property leases to apply an incremental borrowing rate to leases with similar lease terms. The lease terms may include options to extend or terminate the lease. The Company recognizes the options to extend the lease as part of the right-of-use assets and lease liabilities only if it is reasonably certain that the option would be exercised. Lease expense for minimum lease payments is recognized on a straight-line basis over the non-cancelable lease term. Prior period amounts have not been adjusted and continue to be reported in accordance with the Company's historical accounting under previous lease guidance, Topic 840.

As a result of the adoption of the new guidance, the Company recorded a right-of-use asset of $16.2 million, a short-term lease liability of $4.5 million, and a long-term lease liability of $17.0 million and no cumulative effect adjustment was made to the retained earnings as of the adoption date. In addition, as of the adoption date, the Company derecognized a net deferred rent obligation of $5.2 million. See Note 11 for further disclosure.

Recently Issued Accounting Pronouncements

In June 2016, the FASB issued ASU No. 2016-13, Financial Instruments — Credit Losses, *(Topic 326): Measurement of Credit Losses on Financial Instruments*, which changes the impairment model for most financial assets and certain other instruments. For trade receivables and other instruments, the Company will be required to use a new forward-looking expected loss model that generally will result in the earlier recognition of allowances for losses. For available-for-sale debt securities with unrealized losses, the losses will be recognized as allowances rather than as reductions in the amortized cost of the securities. This guidance is effective for the Company on January 1, 2020, and early adoption is permitted. The Company is currently evaluating the effect that this guidance will have on its Consolidated Financial Statements and related disclosures.

3. Financial Instruments

Financial assets and liabilities are recorded at fair value. The carrying amount of certain financial instruments, including cash and cash equivalents, accounts receivable, 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 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 an 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, 2019			
	Level 1	Level 2	Level 3	Total
Money market funds	$ 92,414	$ —	$ —	$ 92,414
Time deposits	—	10,000	—	10,000
Corporate bonds	—	58,742	—	58,742
Commercial paper	—	132,947	—	132,947
Asset-backed securities	—	40,901	—	40,901
U.S. Government Treasury and agency securities	112,200	157,135	—	269,335
Investment in Arcturus equity securities	22,656	—	1,511	24,167
Total	$ 227,270	$ 399,725	$ 1,511	$ 628,506

	December 31, 2018			
	Level 1	Level 2	Level 3	Total
Money market funds	$ 72,999	$ —	$ —	$ 72,999
Time deposits	—	10,000	—	10,000
Corporate bonds	—	179,926	—	179,926
Commercial paper	—	50,198	—	50,198
Asset-backed securities	—	22,587	—	22,587
U.S. Government Treasury and agency securities	—	99,034	—	99,034
Total	$ 72,999	$ 361,745	$ —	$ 434,744

The Company determines the fair value of the Arcturus common stock by using the quoted market price on June 30, 2019, which is a Level 1 fair value measurement. The change in fair value of the Arcturus common stock for the three and six months ended June 30, 2019 was $8.8 million, which was recognized in the Condensed Consolidated Statements of Operations.

The fair value of the option to purchase additional shares of Arcturus common stock was based on unobservable inputs that are significant to the measurement of the fair value of the asset and is supported by little or no market data; accordingly, the fair value of the option is considered a Level 3 financial asset. The Company measures the Level 3 financial asset by applying the Black-Scholes option pricing method and utilizes the following inputs: stock price, strike price, volatility, risk free interest rate, and expected term. The expected term is the Company's estimated period to purchase additional stock. The change in fair value of the option to purchase additional Arcturus common stock for the three and six months ended June 30, 2019 was $1.0 million, which was recognized in the Condensed Consolidated Statements of Operations.

See "Note 6. License and Research Agreement" for additional details on the Arcturus transaction.

4. Balance Sheet Components

Cash Equivalents and Investments

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

	June 30, 2019			
		Gross Unrealized		
	Amortized Cost	Gains	Losses	Estimated Fair Value
Money market funds	$ 92,414	$ —	$ —	$ 92,414
Time deposits	10,000	—	—	10,000
Corporate bonds	58,692	50	—	58,742
Commercial paper	132,947	—	—	132,947
Asset-backed securities	40,834	67	—	40,901
U.S. Government Treasury and agency securities	269,023	312	—	269,335
Total	$ 603,910	$ 429	$ —	$ 604,339

	December 31, 2018			
		Gross Unrealized		
	Amortized Cost	Gains	Losses	Estimated Fair Value
Money market funds	$ 72,999	$ —	$ —	$ 72,999
Time deposits	10,000	—	—	10,000
Corporate bonds	180,167	—	(241)	179,926
Commercial paper	50,198	—	—	50,198
Asset-backed securities	22,597	—	(10)	22,587
U.S. Government Treasury and agency securities	99,087	2	(55)	99,034
Total	$ 435,048	$ 2	$ (306)	$ 434,744

At June 30, 2019, the remaining contractual maturities of available-for-sale securities were less than one year. There have been no material realized gains or losses on available-for-sale securities for the periods presented.

Inventory

Inventory consists of the following (in thousands):

	June 30, 2019	December 31, 2018
Work-in-progress	$ 11,064	$ 5,384
Finished goods	2,568	1,681
Total inventory	$ 13,632	$ 7,065

Accrued Liabilities

Accrued liabilities consist of the following (in thousands):

	June 30, 2019	December 31, 2018
Research, clinical study, and manufacturing expenses	$ 18,932	$ 16,912
Payroll and related expenses	28,998	36,443
Other	11,334	9,095
Total accrued liabilities	$ 59,264	$ 62,450

5. Revenue

The following table disaggregates total revenues from external customers by collaboration and license revenue and product sales (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
Collaboration and license revenue:				
KKC (Crysvita)	$ 19,179	$ 1,577	$ 33,133	$ 1,592
Bayer	68	8,942	352	18,289
Total collaboration and license revenue	19,247	10,519	33,485	19,881
Product sales:				
Crysvita	1,006	26	1,594	26
Mepsevii	3,240	2,007	5,913	3,126
UX007	656	242	1,329	438
Total product sales	4,902	2,275	8,836	3,590
Total revenues	$ 24,149	$ 12,794	$ 42,321	$ 23,471

The following table disaggregates total revenues based on geographic location (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
United States	$ 20,163	$ 11,838	$ 34,618	$ 21,852
Europe	2,821	930	5,732	1,593
All other	1,165	26	1,971	26
Total revenues	$ 24,149	$ 12,794	$ 42,321	$ 23,471

The following table presents changes in the contract assets (liabilities) (in thousands):

	Six Months Ended June 30,	
	2019	2018
Balance of contract assets (liabilities) at beginning of period	$ 2,979	$ (5,986)
Additions	352	18,877
Deductions	(3,386)	(14,135)
Balance of contract liabilities at end of period	$ (55)	$ (1,244)

The Company's largest accounts receivable balance accounted for 92% and 88% of the total accounts receivable balance as of June 30, 2019 and December 31, 2018, respectively, and was due from a collaboration partner.

6. License and Research Agreements

Kyowa Kirin Collaboration and License Agreement

In August 2013, the Company entered into a collaboration and license agreement with Kyowa Kirin Co., Ltd. (KKC or formerly Kyowa Hakko Kirin Co., Ltd. or KHK). Under the terms of this collaboration and license agreement, as amended, the Company and KKC will collaborate on the development and commercialization of Crysvita in the field of orphan diseases in the United States and Canada, or the profit share territory, and in the European Union and Switzerland, 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 KKC, the Company will be the lead party for development activities in the profit share territory and in the European territory until the applicable transition dates; the Company will also be the lead party for core development activities conducted in Japan and Korea, for which the core development plan is limited to clinical trials mutually agreed to by the Company and KKC. 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 KKC, and KKC shall be responsible for 100% of the costs for development activities in Japan and Korea. On the applicable transition dates in the profit share territory and the European territory, KKC 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 KKC. Crysvita was approved in the European Union in February 2018 and was approved by the FDA in April 2018.

The collaboration and license agreements are within the scope of ASC 808, which provides guidance on the presentation and disclosure of collaborative arrangements.

Collaboration revenue related to sales in profit share territory

The Company and KKC share commercial responsibilities and profits in the profit share territory until the applicable transition date. Under the collaboration agreement, KKC will manufacture and supply Crysvita for commercial use in the profit share territory. The remaining profit or loss after supply costs from commercializing products in the profit-share territory, until the applicable transition date, are shared between the Company and KKC on a 50/50 basis. Thereafter, the Company will be entitled to receive a tiered double-digit revenue share in the mid-to-high 20% range.

The Company is considered the agent in the profit share territory as KKC controls the product before transfer to the customers and has the ability to direct the use of and obtain substantially all of the remaining benefits from the product. The Company recognizes a pro-rata share of collaboration revenue, net of supply costs, in the period the sale occurs. The Company concluded that its portion of KKC's sales in the profit share territory is analogous to a royalty and therefore recorded its share as collaboration revenue, similar to a royalty.

Royalty revenue related to sales in European territory

KKC has the commercial responsibility for Crysvita in the European territory. The Company receives a royalty of up to 10% on net sales in the European territory, which is recognized as the underlying sales occur.

The Company's share of collaboration revenue related to Crysvita was as follows (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
Company's share of collaboration revenue in profit share territory	$ 17,248	$ 1,065	$ 29,187	$ 1,065
Royalty revenue in European territory	1,931	512	3,946	527
Total	$ 19,179	$ 1,577	$ 33,133	$ 1,592

Product revenue related to sales in other territories

The Company is responsible for commercializing Crysvita in Latin America and Turkey. The Company is considered the principal in the arrangement as the Company controls the product before it is transferred to the customer. Accordingly, the Company records revenue on a gross basis related to the sale of Crysvita once the product is delivered and the risk and title of the product is transferred to the distributor. For the three and six months ended June 30, 2019, the Company recorded product sales of $1.0 million and $1.6 million, respectively, net of estimated product returns and other deductions. The Company recorded a nominal amount of product sales for the three and six months ended June 30, 2018.

Under the collaboration agreement, KKC manufactures and supplies Crysvita, which is purchased by the Company for sales in the above territories. The Company also pays to KKC a low single-digit royalty on net sales in Latin America.

One of the wholly-owned subsidiaries of KKC has the option to assume responsibility for commercialization efforts in Turkey from the Company, after a certain minimum period.

Cost sharing payments

Under the collaboration agreement, KKC and the Company shares certain development and commercialization costs. As a result, the Company was reimbursed for these costs and operating expenses were reduced as follows (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
Research and development	$ 5,895	$ 9,420	$ 12,994	$ 17,656
Selling, general and administrative	5,163	4,068	10,376	7,850
Total	$ 11,058	$ 13,488	$ 23,370	$ 25,506

Collaboration receivable

The Company had accounts receivable from KKC in the amount of $19.3 million and $11.2 million, from profit share revenue and royalties, and other receivables recorded in prepaid and other current assets of $13.8 million and $11.1 million from commercial and development activity reimbursements, as of June 30, 2019 and December 31, 2018, respectively.

Bayer HealthCare LLC

The Company has an agreement with Bayer Healthcare LLC (Bayer) to research, develop and commercialize AAV gene therapy products for treatment of hemophilia A (DTX 201). Under this agreement, Bayer has been granted an exclusive license to develop and commercialize one or more novel gene therapies for hemophilia A. The agreement requires that Bayer use commercially reasonable

efforts to conduct and fund a proof-of-concept (POC) clinical trial and any subsequent clinical trials and commercialization of gene therapy products for treatment of hemophilia A. Bayer will have worldwide rights to commercialize the potential future product.

Bayer is responsible to fund certain research and development services performed by the Company in the performance of its obligations under the annual research plan and budget. Under the terms of the agreement with Bayer, the Company is eligible to receive development and commercialization milestone payments of up to $232.0 million, as well as, royalty payments ranging in the high single-digit to low double-digit percentages, not exceeding the mid-teens, of net sales of licensed products. The Company achieved the first milestone in December 2017, the second milestone in April 2018, and has received $15.0 million for such milestones to date.

As of the acquisition date of Dimension Therapeutics, Inc. on November 7, 2017, the Company valued the Bayer contract under ASC 805, *Business Combinations*, and recorded an intangible asset of $13.5 million. The intangible asset is being amortized to research and development expense over the research term which is expected to be complete in 2019. The Company recorded research and development expense of $0.1 million and $0.2 million for the three and six months ended June 30, 2019, respectively, and $4.4 million and $8.8 million for the three and six months ended June 30, 2018, respectively, for the amortization of the intangible asset.

The Company evaluated the agreement under ASC 606 and recorded a contract liability as of November 7, 2017 of $2.5 million. It was determined that the performance obligations under the agreement include (i) research and development services to be provided over the research term, (ii) a development and commercialization license, and (iii) the Company's participation in certain committees. It was determined that these performance obligations are not distinct in the context of the contract and therefore are a single performance obligation. The Company calculated the transaction price by including the unconstrained milestones along with the estimated payments for research and development services and recorded $0.1 million and $0.4 million as collaboration and license revenue for the three and six months ended June 30, 2019, respectively, and $9.0 million and $18.3 million for the three and six months ended June 30, 2018, respectively, by measuring the progress toward complete satisfaction of the performance obligation using an input measure. The performance obligation under the contract is expected to be substantially complete by end of 2019. As of June 30, 2019 and December 31, 2018, the Company had a $0.1 million contract liability and a $3.0 million contract asset, respectively.

Arcturus

The Company has a Research Collaboration and License Agreement with Arcturus to research and develop therapies for select rare diseases. Pursuant to the agreement, the Company incurred $0.4 million and $0.6 million for the three and six months ended June 30, 2019, respectively, and $0.5 million and $0.9 million for the three and six months ended June 30, 2018, respectively, in research and development expense for the funding of certain research services received from Arcturus. As of June 30, 2019 and December 31, 2018, the Company has a balance of none and $0.5 million, respectively, in prepaid expenses and other current assets, and a balance of none and $0.4 million, respectively, in accrued liabilities related to Arcturus.

In June 2019, the Company entered into an Equity Purchase Agreement and an amendment to the Research Collaboration and License Agreement to expand the field of use and increase the number of disease targets to include mRNA, DNA and siRNA therapeutics for up to 12 rare diseases. Pursuant to the agreements, the Company paid $6.0 million in cash upfront to Arcturus and purchased 2,400,000 shares of Arcturus' common stock at a stated value of $10.00 per share, resulting in a total of $30.0 million of consideration paid at the close of the transaction. As a result, the Company received expanded license rights; the Arcturus common stock; an option to purchase an additional 600,000 shares of Arcturus' common stock at $16.00 per share, which may be exercised up to two years after the agreement effective date, with certain restrictions; in addition to other changes as noted in the agreement. The period for the Company to exercise its option to purchase the additional stock may also be extended under certain circumstances as specified in the Equity Purchase Agreement. The Company is restricted from selling the 2,400,000 shares of common stock for a period of two years from the purchase date. The additional stock, if purchased, are also restricted from sale for a period of time as specified in the agreement. The Company also received the right to nominate one member to the Arcturus Board of Directors as well as one Board observer. Under the amended license agreement, certain early-stage milestone payments are reduced and the total potential milestone payments are increased due to the expanded number of targets. Arcturus is also entitled to reimbursement of related research expenses and royalties on commercial sales.

Immediately after the purchase, the Company held 18.2% of Arcturus' outstanding common stock, based on Arcturus' outstanding common stock balance as of the transaction date. The Company recorded the common stock investment at $13.9 million on the transaction date, which was based on the quoted market price on the closing date. As a result of the equity ownership and the right to nominate a board member, it was determined that the Company has significant influence over Arcturus. The Company elected to apply the fair value option to account for the equity investment in Arcturus. The Company also accounts for the option to purchase additional shares of Arcturus common stock at fair value, which was recorded at $0.5 million on the transaction date based on the Black-Scholes option pricing method. The remaining $15.6 million of the total $30.0 million paid as consideration was attributed to the additional license rights obtained and was recorded as in-process research and development expense.

For the three and six months ended June 30, 2019, the Company recorded an increase in the fair value of Arcturus common stock of $8.8 million and an increase in fair value of the option to purchase additional shares of Arcturus common stock of $1.0 million in its Condensed Consolidated Statement of Operations. As of June 30, 2019, the fair value of the Company's investment in

Arcturus common stock was $22.7 million based on the quoted market price on that date and the fair value of the Company's option to purchase additional shares of Arcturus common stock was $1.5 million based on the Black-Scholes option pricing method.

7. Stock-Based Awards

The 2014 Incentive Plan (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, 2019, there were 2,582,049 shares reserved under the 2014 Plan for the future issuance of equity awards and 2,740,058 shares reserved for the 2014 Employee Stock Purchase Plan.

The table below sets forth the stock-based compensation expense for the periods presented (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
Cost of sales	$ 51	$ —	$ 85	$ —
Research and development	12,032	11,644	23,262	22,891
Selling, general and administrative	10,124	7,919	19,081	15,469
Total stock-based compensation expense	$ 22,207	$ 19,563	$ 42,428	$ 38,360

8. 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,	
	2019	2018	2019	2018
Options to purchase common stock and restricted stock units	8,220,733	7,735,231	7,825,615	7,479,526
Employee stock purchase plan	7,857	9,369	3,950	4,710
Common stock warrants	149,700	149,700	149,700	149,700
	8,378,290	7,894,300	7,979,265	7,633,936

9. Equity Transactions

In July 2017, the Company entered into an At-The-Market, or ATM, sales agreement with Cowen and Company, LLC (Cowen), whereby the Company can sell up to $150.0 million in aggregate proceeds of common stock from time to time, through with Cowen as its sales agent. During the three and six months ended June 30, 2019, the Company sold 88,978 and 468,685 shares of common stock, respectively, resulting in net proceeds of approximately $5.5 million and $24.8 million, respectively, after commissions and other offering costs. During the three and six months ended June 30, 2018, the Company sold 240,417 shares of common stock, resulting in net proceeds of approximately $11.8 million after commissions and other offering costs.

In February 2019, the Company completed an underwritten public offering in which 5,833,333 shares of common stock were sold, which included 760,869 shares purchased by the underwriters pursuant to an option granted to them in connection with the offering, at a public offering price of $60.00 per share. The total proceeds that the Company received from the offering were approximately $330.4 million, net of underwriting discounts and commissions.

10. Accumulated Other Comprehensive Income (Loss)

Total accumulated other comprehensive income (loss) consisted of the following (in thousands):

	June 30, 2019	December 31, 2018
Foreign currency translation adjustments	$ (174)	$ (329)
Unrealized gain (loss) on securities available-for-sale	429	(304)
Total accumulated other comprehensive income (loss)	$ 255	$ (633)

11. Leases

As described in “Note 2. Summary of Significant Accounting Policies”, the Company adopted *Topic 842* as of January 1, 2019. Prior period amounts have not been adjusted and continue to be reported in accordance with historic accounting under *Topic 840*.

The Company leases office space and research, testing and manufacturing laboratory space in various facilities in Novato and Brisbane, California, in Cambridge and Woburn, Massachusetts, and in certain foreign countries, under operating agreements expiring at various dates through 2028. Certain of the leases provide for options by the Company to extend the lease for multiple five-year renewal periods and also provide for annual minimum increases in rent, usually based on a consumer price index or annual minimum increases. None of these optional periods have been considered in the determination of the right-of-use asset or the lease liability for the leases as the Company did not consider it reasonably certain that it would exercise any such options. The Company recognizes lease expense on a straight-line basis over the non-cancelable term of its operating leases. The variable lease expense primarily consists of common area maintenance and other operating costs.

The components of lease expense were as follows (in thousands):

	Three Months Ended June 30, 2019	Six Months Ended June 30, 2019
Operating lease expense	$ 2,373	$ 4,330
Variable lease expense	669	1,321
Total lease expense	$ 3,042	$ 5,651

Cash paid for amounts included in the measurement of lease liabilities for the three and six months ended June 30, 2019 was $2.2 million and $4.2 million, respectively, and was included in net cash provided by operating activities in the Consolidated Statements of Cash Flows.

Future minimum lease payments under non-cancellable leases as of June 30, 2019 were as follows (in thousands):

Year Ending December 31,	Leases
2019 (remaining)	$ 4,724
2020	9,639
2021	7,561
2022	7,433
2023	7,541
Thereafter	13,153
Total future lease payments	50,051
Less: Amount representing interest	(10,084)
Present value of future lease payments	$ 39,967
Less: Short-term lease liabilities	(6,999)
Long-term lease liabilities	$ 32,968

Lease liabilities are based on the net present value of the remaining lease payments over the remaining lease term. As of June 30, 2019, the weighted-average remaining lease term was 5.98 years and the weighted-average discount rate used to determine the lease liability was 7.5%.

12. Gain from Sale of Priority Review Vouchers

In January 2018, the Company completed the sale of a Rare Pediatric Disease Priority Review Voucher (PRV) it received in connection with the approval of Mepsevii for $130.0 million. In June 2018, the Company also completed the sale of the PRV it received in connection with the approval of Crysvita for $80.6 million, net, which was shared equally with KKC. As the PRVs did not have a carrying value, the gain recognized was equal to the net proceeds received. The Company recorded its portion of the net proceeds in other income of $40.3 million and $170.3 million for the three and six months ended June 30, 2018, respectively, as a gain from the sale of the PRVs.

Item 2. ***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, 2018 (the "Annual Report").

Overview

Ultragenyx Pharmaceutical Inc. (we or the Company) is a biopharmaceutical company focused on the identification, acquisition, development, and commercialization of novel products for the treatment of serious rare and ultra-rare 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. 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.

Approved Therapies and Clinical Product Candidates

Our current approved therapies and clinical-stage pipeline consist of three product categories: biologics, small molecules, and gene therapy product candidates.

Our biologic products include approved therapies Crysvita® (burosumab) and Mepsevii® (vestronidase alfa):

- Crysvita is an antibody targeting fibroblast growth factor 23, or FGF23, developed for the treatment of X-linked hypophosphatemia, or XLH, a rare, hereditary, progressive and lifelong musculoskeletal disorder characterized by renal phosphate wasting caused by excess FGF23 production. Crysvita is approved in the United States and Canada for the treatment of XLH in adult and pediatric patients one year of age and older. In the European Union, or EU, Crysvita is conditionally approved for the treatment of XLH with radiographic evidence of bone disease in children one year of age and older and adolescents with growing skeletons. A filing to expand the label to include adults with XLH is also planned in the EU. In Brazil, Crysvita is approved for treatment of XLH in adult and pediatric patients one year of age and older. We have submitted regulatory filings in various other Latin American countries.

  We are collaborating with Kyowa Kirin Co., Ltd., or KKC (formerly Kyowa Hakko Kirin Co., Ltd., or KHK), and Kyowa Kirin International, or Kyowa Kirin, a wholly owned subsidiary of KKC, on the development and commercialization of Crysvita globally. A regulatory submission to expand the label to include adults with XLH is also planned by our partner, Kyowa Kirin, in the EU.

  Crysvita 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.
- Mepsevii is an intravenous, or IV, enzyme replacement therapy, developed for the treatment of Mucopolysaccharidosis VII, also known as MPS VII or Sly syndrome, a rare lysosomal storage disease that often leads to multi-organ dysfunction, pervasive skeletal disease, and death. Mepsevii is approved in the United States for the treatment of children and adults with MPS VII. In the EU, Mepsevii is approved under exceptional circumstances for the treatment of non-neurological manifestations of MPS VII for patients of all ages. In Brazil, Mepsevii is approved for the treatment of MPS VII for patients of all ages.

Our small molecule pipeline includes UX007, which is in clinical development for the treatment of long-chain fatty acid oxidation disorders, or LC-FAOD:

- UX007 is a synthetic triglyceride with a specifically designed chemical composition being studied for the treatment of LC-FAOD, which 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. We have submitted a new drug application, or NDA, to the U.S. Food and Drug Administration, or FDA, for the treatment of LC-FAOD. We are also continuing discussions with EU regulatory authorities.

Our gene therapy pipeline includes DTX301 and DTX401 in clinical development for the treatment of two diseases:

- DTX301 is an adeno-associated virus 8, or AAV8 gene therapy product candidate designed for the treatment of patients with ornithine transcarbamylase, or OTC, deficiency. OTC is part of the urea cycle, an enzymatic pathway in the liver that converts excess nitrogen, in the form of ammonia, to urea for excretion. OTC deficiency is the most common urea cycle disorder and leads to increased levels of ammonia. Patients with OTC deficiency suffer from acute hyperammonemic episodes that can lead to hospitalization, adverse cognitive and neurological effects, and death. We have reported positive data from the first and second dose cohorts of the Phase 1/2 study, with two responders maintaining normalized rates of ureagenesis through 52 weeks and 78 weeks.
- DTX401 is an AAV8 gene therapy clinical candidate for the treatment of patients with glycogen storage disease type Ia, or GSDIa, a disease that arises from a defect in G6Pase, an essential enzyme in glycogen and glucose metabolism. GSDIa is the most common glycogen storage disease. We have reported positive data from the first dose cohort of the Phase 1/2 study,

with all three patients showing a clinical response with improvements in glucose control reflected by prolonged time to hypoglycemia during a controlled fasting challenge at 24 weeks.

- We expect to provide an update on the third dose cohort of the DTX301 study and the second dose cohort of the DTX401 study in the third quarter of 2019.

The following table summarizes our approved products and clinical product candidate pipeline:

Recent program updates

Clinical Product Candidates

UX007 for the treatment of Long Chain Fatty-Acid Oxidation Disorders, or LC-FAOD

In August 2019, we announced that we submitted an NDA for UX007 for the treatment of LC-FAOD. The submission includes data from a company-sponsored Phase 2 study of UX007 in 29 patients, data from a long-term safety and efficacy extension study in 75 patients including 20 patients previously naïve to UX007, a retrospective medical record review of 20 original compassionate use patients, data from 67 patients treated through expanded access, and a randomized controlled investigator-sponsored study of 32 patients showing an effect on cardiac function. We expect to hear back from FDA regarding submission acceptance within 60 days of the NDA submission.

In April 2019, we announced that the FDA has granted Fast Track designation and Rare Pediatric Disease designation to UX007 for the treatment of LC-FAOD. Fast Track designation enables eligibility for Priority Review, if relevant criteria are met.

Preclinical program updates

Expansion of Research Collaboration and License Agreement with Arcturus Therapeutics Holdings Inc.

In June 2019, we announced the expansion of our research and collaboration arrangement with Arcturus Therapeutics Holdings Inc., or Arcturus, to discover and develop mRNA, DNA and siRNA therapeutics for up to 12 rare disease targets pursuant to the terms of an amendment to the Research Collaboration and License Agreement, or License Agreement, and Equity Purchase Agreement. In connection with the amendment to the License Agreement, we made a $6.0 million cash upfront payment to Arcturus and also purchased 2,400,000 shares of Arcturus' common stock at a stated value of $10.00 per share. We have an option to purchase an additional 600,000 shares of Arcturus' common stock at $16.00 per share. Arcturus is entitled to preclinical, clinical, regulatory, and

sales milestone payments for each product developed under the collaboration. Under the amended license agreement, certain early-stage milestone payments are reduced and the total potential milestone payments are increased due to the expanded number of targets. Arcturus is also entitled to reimbursement of related research expenses and royalties on commercial sales. The original collaboration and license agreement between the Company and Arcturus was signed in October 2015. The two parties have been working together to develop mRNA therapeutic candidates for certain rare disease targets. The first disclosed indication under the collaboration is Glycogen Storage Disease Type III, and an Investigational New Drug, or IND, application for this mRNA therapeutic program, UX053, is expected to be filed in 2020.

Other Developments

In June 2019, we promoted Erik Harris to Executive Vice President and Chief Commercial Officer, responsible for all commercial operations in North America, Europe, and Latin America. Mr. Harris joined Ultragenyx in 2017 as Senior Vice President, Head of North American Commercial Operations.

Financial Operations Overview

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

We have incurred net losses in each year since inception. Our net loss was $99.2 million and $195.9 million for the three and six months ended June 30, 2019 and our net loss was $52.7 million and $22.5 million for the three and six months ended June 30, 2018, respectively. Net loss for the three and six months ended June 30, 2018 included the gain from the sale of priority review vouchers, or PRVs, of $40.3 million and $170.3 million, respectively, received from the FDA in connection with the approval of Mepsevii and Crysvita. Substantially all of our net losses have resulted from costs incurred in connection with our research and development programs and from selling, general and administrative costs associated with our operations.

We record revenue from our collaboration and license agreements and from the sale of our two approved products – Crysvita and Mepsevii. In addition, we also record sales of certain products on a “named patient” basis, which are allowed in certain countries prior to regulatory approval. For the three and six months ended June 30, 2019, we recorded $19.2 million and $33.1 million, respectively, and for the three and six months ended June 30, 2018, we recorded $1.6 million in collaboration and license revenue for Crysvita sales. For the three and six months ended June 30, 2019, we recorded $0.1 million and $0.4 million, respectively, and for the three and six months ended June 30, 2018, we recorded $8.9 million and $18.3 million, respectively, for providing certain research and development services under our collaboration and license arrangement with Bayer Healthcare LLC, or Bayer. For the three and six months ended June 30, 2019, we recorded $4.9 million and $8.8 million, respectively, and for the three and six months ended June 30, 2018, we recorded $2.3 million and $3.6 million, respectively, in product sales from our approved products and named patient sales in certain countries.

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 consolidated financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles, or GAAP. The preparation of these 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 material changes in our critical accounting policies, except as noted below with respect to our investment in equity securities, during the six months ended June 30, 2019, 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 Annual Report.

Investment in Equity Securities

Our investment in equity securities in Arcturus is accounted for using the equity method of accounting as we have determined that we have significant influence over, but do not control the significant activities of Arcturus. We have elected to apply the fair value option to account for the equity investments in Arcturus at the time the securities were purchased and such securities will continue to be adjusted to fair value at each reporting period. The decision to elect the fair value option is irrevocable and is determined on an instrument by instrument basis. The investment in common stock is accounted for at fair value based upon the current then current stock price. The option to purchase additional stock is accounted for at fair value using Black-Scholes option pricing method and utilizes the following inputs: stock price, strike price, volatility, risk free interest rate, and expected term. The expected term is the Company’s estimated period to purchase additional stock. The sensitivity of these inputs to the fair value of the equity security is

assessed on a periodic basis. The changes in fair value of the equity investment and option to purchase additional stock is included in the Condensed Consolidated Statements of Operations.

Results of Operations

Comparison of the three and six months ended June 30, 2019 to the three and six months ended June 30, 2018:

Revenue (dollars in thousands)

	Three Months Ended June 30,		Dollar	%
	2019	2018	Change	Change
Collaboration and license revenue:				
KKC (Crysvita)	$ 19,179	$ 1,577	$ 17,602	*
Bayer	68	8,942	(8,874)	-99%
Total collaboration and license revenue	19,247	10,519	8,728	83%
Product sales:				
Crysvita	1,006	26	980	*
Mepsevii	3,240	2,007	1,233	61%
UX007	656	242	414	171%
Total product sales	4,902	2,275	2,627	115%
Total revenues	$ 24,149	$ 12,794	$ 11,355	89%

* not meaningful

	Six Months Ended June 30,		Dollar	%
	2019	2018	Change	Change
Collaboration and license revenue:				
KKC (Crysvita)	$ 33,133	$ 1,592	$ 31,541	*
Bayer	352	18,289	(17,937)	-98%
Total collaboration and license revenue	33,485	19,881	13,604	68%
Product sales:				
Crysvita	1,594	26	1,568	*
Mepsevii	5,913	3,126	2,787	89%
UX007	1,329	438	891	203%
Total product sales	8,836	3,590	5,246	146%
Total revenues	$ 42,321	$ 23,471	$ 18,850	80%

The increases of $17.6 million and $31.5 million in profit sharing and royalty revenue from our collaboration and license agreement with KKC for the three and six months ended June 30, 2019, respectively, compared to the same periods in 2018, were as a result of the approval of Crysvita in Europe in November 2017 and in the U.S. in April 2018.

The decreases of $8.9 million and $17.9 million in collaboration and license revenue from our research arrangement with Bayer for the three and six months ended June 30, 2019, respectively, compared to the same periods in 2018, were due to the transition of the clinical development to Bayer as part of the research arrangement.

The increases in product sales of $2.6 million and $5.2 million for the three and six months ended June 30, 2019 compared to the same periods in 2018 were primarily due to the approval of Mepsevii in November 2017 resulting in an increase in sales in the U.S. and increase in sales of certain products under our named patient program in certain countries.

Cost of Sales (dollars in thousands)

	Three Months Ended June 30,		Dollar	%
	2019	2018	Change	Change
Cost of sales	$ 766	$ 141	$ 625	443%

	Six Months Ended June 30,		Dollar	%
	2019	2018	Change	Change
Cost of sales	$ 1,218	$ 366	$ 852	233%

We recognized increases of $0.6 million and $0.9 million in cost of sales related to our approved products for the three and six months ended June 30, 2019, compared to the same periods in 2018. The cost of sales included a reserve for excess inventory of $0.2 million for the three and six months ended June 30, 2018. There was no reserve for excess inventory recorded for the three and six

months ended June 30, 2019. Prior to the approval of our approved products, manufacturing and related costs were expensed; accordingly, these costs were not capitalized and as a result are not fully reflected in the costs of sales during the current period. If manufacturing and related costs were capitalized prior to the approval period, we estimate that cost of sales for the three and six months ended June 30, 2019 would have been approximately $1.0 million and $1.7 million, respectively, and for the three and six months ended June 30, 2018 would have been approximately $0.5 million and $0.9 million, respectively, for our commercial product sales. We expect our gross margin percentage to decrease as we produce Mepsevii at costs that reflect the full costs of manufacturing similar biologic products and as we deplete inventories that we had expensed prior to receiving FDA approval.

Research and Development Expenses (dollars in thousands)

	Three Months Ended June 30,		Dollar	%
	2019	2018	Change	Change
Crysvita	$ 10,210	$ 12,037	$ (1,827)	-15%
Mepsevii	4,197	7,030	(2,833)	-40%
UX007	10,407	11,349	(942)	-8%
DTX301	7,722	4,751	2,971	63%
DTX401	7,581	4,139	3,442	83%
DTX201	481	9,380	(8,899)	-95%
Translational Research	15,127	6,080	9,047	149%
Other research costs	40,320	22,069	18,251	83%
Total research and development expenses	$ 96,045	$ 76,835	$ 19,210	25%

	Six Months Ended June 30,		Dollar	%
	2019	2018	Change	Change
Crysvita	$ 20,531	$ 23,260	$ (2,729)	-12%
Mepsevii	9,655	13,363	(3,708)	-28%
UX007	22,775	23,292	(517)	-2%
DTX301	19,849	8,177	11,672	143%
DTX401	16,393	10,097	6,296	62%
DTX201	1,261	19,340	(18,079)	-93%
Translational Research	25,017	13,599	11,418	84%
Other research costs	58,669	41,211	17,458	42%
Total research and development expenses	$ 174,150	$ 152,339	$ 21,811	14%

Research and development expenses increased $19.2 million and $21.8 million for the three and six months ended June 30, 2019, respectively, compared to the same periods in 2018. The increase in research and development expenses was primarily due to:

- for Crysvita, a decrease of $1.8 million and $2.7 million for the three and six months ended June 30, 2019, respectively, primarily related to reduced clinical trial activity with the progressive completion of our extension studies and reduced allocation of employees and contractors to R&D support activities, net of KKC reimbursement;
- for Mepsevii, a decrease of $2.8 million and $3.7 million for the three and six months ended June 30, 2019, respectively, primarily related to reduced clinical trial activity with the progressive completion of our extension studies;
- for UX007, a decrease of $0.9 million and $0.5 million for the three and six months ended June 30, 2019, respectively, primarily related to the reduced clinical trial expense for the wind down of the Glut 1 program and reduced manufacturing expense due to the timing of drug substance campaigns, net of increased filing preparation expense for the LC-FAOD program;
- for DTX301, an increase of $3.0 million and $11.7 million for the three and six months ended June 30, 2019, respectively, primarily related to increases in manufacturing and quality activities in support of our clinical development program;
- for DTX401, an increase of $3.4 million and $6.3 million for the three and six months ended June 30, 2019, respectively, related to clinical manufacturing expense process development expense, and the progressive enrollment of our Phase 1/2 clinical study;
- for DTX201, a decrease of $8.9 million and $18.1 million for the three and six months ended June 30, 2019, respectively, primarily related to the completion of clinical manufacturing and regulatory support activities for our Bayer collaboration agreement and the corresponding period decrease in intangible asset amortization;
- for translational research, an increase of $9.0 million and $11.4 million for the three and six months ended June 30, 2019, respectively, primarily related to research, process development, and manufacturing activities, including the progression of UX701, UX053, and UX068 toward IND filings; and

- for other research and development costs, an increase of $18.3 million and $17.5 million for the three and six months ended June 30, 2019, respectively, primarily due to the $15.6 million recorded for the consideration attributable to the amended Research Collaboration and License Agreement in connection with the Arcturus transaction in June 2019, as well as increases in general operating and overhead expenses in support of our clinical and research program pipeline, net of reduced operating expense for terminated programs.

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.

Selling, General and Administrative Expenses (dollars in thousands)

	Three Months Ended June 30,		Dollar	%
	2019	2018	Change	Change
Selling, general and administrative	$ 39,812	$ 30,718	$ 9,094	30%

	Six Months Ended June 30,		Dollar	%
	2019	2018	Change	Change
Selling, general and administrative	$ 78,641	$ 62,153	$ 16,488	27%

Selling, general and administrative expenses increased $9.1 million and $16.5 million for the three and six months ended June 30, 2019, respectively, compared to the same periods in 2018. The increase in selling, general and administrative expenses was primarily due to increases in personnel costs resulting from an increase in the number of employees in support of our commercial activities, stock-based compensation, commercialization costs, and professional services costs.

We expect selling, general and administrative expenses to increase in the future to support our organizational growth and for our expected staged build out of our commercial organization over the next several years related to our approved products and multiple clinical-stage product candidates.

Interest Income (dollars in thousands)

	Three Months Ended June 30,		Dollar	%
	2019	2018	Change	Change
Interest income	$ 4,063	$ 2,448	$ 1,615	66%

	Six Months Ended June 30,		Dollar	%
	2019	2018	Change	Change
Interest income	$ 7,149	$ 4,185	$ 2,964	71%

Interest income increased $1.6 million and $3.0 million for the three and six months ended June 30, 2019, respectively, compared to the same periods in 2018, primarily due to an increase in the balance of our invested funds and due to an increase in yields on our investment portfolio.

Gain from Sale of Priority Review Voucher (dollars in thousands)

	Three Months Ended June 30,		Dollar	%
	2019	2018	Change	Change
Gain from sale of priority review vouchers	$ —	$ 40,322	$ (40,322)	-100%

	Six Months Ended June 30,		Dollar	%
	2019	2018	Change	Change
Gain from sale of priority review vouchers	$ —	$ 170,322	$ (170,322)	-100%

The gain from the sale of the PRVs of $40.3 million and $170.3 million for the three and six months ended June 30, 2018, respectively, was due to the completion of the sales of the PRVs we received from the FDA in connection with the approval of Crysvita and Mepsevii. The Crysvita PRV was sold in April 2018 for net proceeds of $80.6 million, which was shared equally with KKC, and the Mepsevii PRV was sold in January 2018 for net proceeds of $130.0 million.

Investment in Arcturus Equity Securities (dollars in thousands)

The increase of our investment in Arcturus equity securities of $9.8 million for the three and six months ended June 30, 2019 was due to the initial fair value at the time of our purchase of Arcturus common stock and option to purchase additional Arcturus stock on June 18, 2019 and the remeasurement of these securities at fair value at June 30, 2019. Given the historic volatility of the publically

traded stock price of Arcturus, we expect the fair value adjustments of our investments in Arcturus to be subject to wide fluctuations which may have a significant impact on the fair value of our investment in Arcturus equity securities at each reporting period.

Other Expense (dollars in thousands)

	Three Months Ended June 30,		Dollar	%
	2019	2018	Change	Change
Other expense	$ (376)	$ (496)	$ 120	-24%

	Six Months Ended June 30,		Dollar	%
	2019	2018	Change	Change
Other expense	$ (788)	$ (5,454)	$ 4,666	(86)%

Other expense decreased $0.1 million and $4.7 million for the three and six months ended June 30, 2019, respectively, compared to the same periods in 2018. The expense recognized during the six months ended June 30, 2018 was primarily due to the recognition of cumulative foreign currency translation losses related to the substantial liquidation of subsidiaries with a functional currency other than the U.S. Dollar, which did not recur in 2019. The recognized foreign currency losses from the six months ended June 30, 2018 were substantially offset by the reclassification adjustment reported as a component of other comprehensive income (loss).

Provision for Income Taxes (dollars in thousands)

	Three Months Ended June 30,		Dollar	%
	2019	2018	Change	Change
Provision for income taxes	$ (213)	$ (102)	$ (111)	109%

	Six Months Ended June 30,		Dollar	%
	2018	2017	Change	Change
Provision for income taxes	$ (429)	$ (141)	$ (288)	204%

The provision for incomes taxes increased $0.1 million and $0.3 million for the three and six months ended June 30, 2019, respectively, compared to the same periods in 2018. This was primarily due to the increase in commercialization activities in Europe and Latin America.

Liquidity and Capital Resources

We have funded our operations primarily from the sale of equity securities.

As of June 30, 2019, we had $618.3 million in available cash, cash equivalents, and available-for-sale investments. We believe that our existing capital resources will be sufficient to fund our projected operating requirements for at least the next twelve months. Our cash, cash equivalents, and available-for-sale investments are held in a variety of deposit accounts, interest-bearing accounts, corporate bond securities, U.S government securities and money market funds. 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.

During the three and six months ended June 30, 2019, the proceeds from our at-the-market, or ATM, offering were approximately $5.5 million and $24.8 million, respectively, after commissions and other offering costs. As of June 30, 2019, $20.7 million remained to be sold under our ATM facility. In February 2019, we completed an underwritten public offering in which we sold 5,833,333 shares of common stock and received net proceeds of approximately $330.4 million.

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

	Six Months Ended June 30,	
	2019	2018
Cash used in operating activities	$ (184,838)	$ (165,556)
Cash used in investing activities	(159,619)	(123,097)
Cash provided by financing activities	362,959	299,587
Effect of exchange rate changes on cash	(30)	(647)
Net increase in cash, cash equivalents and restricted cash	$ 18,472	$ 10,287

Cash Used in Operating Activities

Our primary use of cash is to fund operating expenses, which consist primarily of research and development and commercial 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, 2019 was $184.8 million and reflected a net loss of $195.9 million, $3.0 million for the amortization of the discount paid on purchased investments, and $9.8 million for an increase in fair value of the investment in Arcturus equity securities, offset by non-cash charges of $42.4 million for stock-based compensation, $4.2 million for depreciation and amortization of an intangible asset acquired, and $0.6 million of non-cash foreign currency remeasurement losses in connection with fluctuations of exchange rates related to intercompany transactions with foreign subsidiaries that are denominated in our reporting currency. Cash used in operating activities also reflected a $8.2 million decrease due to an increase in accounts receivable due to the commercialization of Mepsevii and Crysvita, a $6.0 million decrease due to an increase in inventory as we build out our commercial inventory supplies as we commercialize Mepsevii, a decrease of $4.3 million due to an increase in prepaid expenses and other current assets primarily due to an increase in general receivables, amounts due from a collaboration partner, and amounts owed for a tenant improvement allowance, a $17.2 million decrease due to the addition of the right-of-use assets net of amortization during the period, a $3.6 million decrease in accounts payable primarily due to the timing of payments and receipt of invoices, and a $3.4 million decrease in accrued expenses and other liabilities primarily due to a decrease in accrued bonus due to the payout of the 2018 annual bonus, the derecognition of deferred rent obligations for the new lease accounting guidance, and accrued expenses due to the timing of the receipt of invoices, offset by an increase of $1.0 million in other assets and a $18.5 million increase due to the addition of lease liabilities net of amortization during the period.

Cash used in operating activities for the six months ended June 30, 2018 was $165.6 million and reflected a net loss of $22.5 million, $0.9 million for the amortization of the discount paid on purchased investments, and $170.3 million for the gain from sale of the PRVs, offset by non-cash charges of $38.4 million for stock-based compensation, $12.2 million for depreciation and amortization of intangible asset acquired, and $5.8 million of non-cash foreign currency remeasurement losses in connection with the substantial liquidation of subsidiaries due to a change in the Company's tax structure and fluctuations of exchange rates related to intercompany transactions with foreign subsidiaries that are denominated in our reporting currency. Cash used in operating activities also reflected a $12.3 million decrease due to an increase in accounts receivable due to the commercialization of Mepsevii and Crysvita, a $2.6 million decrease due to an increase in inventory as we build out our commercial inventory supplies as we commercialize Mepsevii, a decrease of $7.6 million due to an increase in prepaid expenses and other assets primarily due to prepayments in manufacturing, a $0.1 million decrease due to an increase in other assets, and a $7.0 million decrease in accrued expenses and other liabilities primarily as a result of a decrease in accrued bonus due to the payout of the 2017 annual bonus and accrued expenses due to the timing of the receipt of invoices, offset by a $1.4 million increase in accounts payable primarily due to the timing of payments and receipt of invoices,.

Cash Used in Investing Activities

Cash used in investing activities for the six months ended June 30, 2019 was $159.6 million and related to purchases of investments of $461.1 million, purchases of property and equipment of $8.3 million, and purchases of Arcturus equity securities of $14.3 million, offset by proceeds from maturities of investments of $301.5 million and the sale of investments of $22.6 million.

Cash used in investing activities for the six months ended June 30, 2018 was $123.1 million and related to purchases of property and equipment of $1.9 million and purchases of investments of $408.7 million, offset by the sale of investments of $5.0 million, proceeds from maturities of investments of $112.2 million, and proceeds from the sale of PRVs of $170.3 million.

Cash Provided by Financing Activities

Cash provided by financing activities for the six months ended June 30, 2019 was $363.0 million and was comprised of $330.4 million from the sale of common stock in our underwritten public offering in February 2019, $24.8 million from the sale of common stock in our ATM offering, and $7.7 million in net proceeds from the issuance of common stock pursuant to equity awards.

Cash provided by financing activities for the six months ended June 30, 2018 was $299.6 million and was comprised of $271.0 million from the sale of common stock in our underwritten public offering in January 2018, $11.8 million from the sale of common stock in our ATM offering, and $16.8 million in net proceeds from the issuance of common stock pursuant to equity awards.

Funding Requirements

We anticipate, excluding non-recurring items, that we will continue to generate annual 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 continue with commercialization of approved products. Due to certain non-recurring or infrequent items like the sale of PRVs, we may have lower levels of losses in the near term in quarterly periods that may not be indicative of future periods or trends. We will likely require additional capital to fund our operations, to complete our ongoing and planned clinical studies, to commercialize our products, and to continue investing in early-stage research capabilities to promote our pipeline growth and to further develop our general infrastructure, including building our own Good Manufacturing Practices, or GMP gene therapy manufacturing facility, and such funding may not be available to us on acceptable terms or at all.

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 our commercial infrastructure, and distribution capabilities; and
- the terms and timing of any collaborative, licensing, marketing, distribution, and other arrangements that we may establish, including any required upfront milestone and royalty payments thereunder.

We expect to satisfy future cash needs through existing capital balances and through some combination of public or private equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements, and other marketing and distribution arrangements. Please see “Risk Factors—Risks Related to Our Financial Condition and Capital Requirements.”

Contractual Obligations and Commitments

We have contractual obligations from our operating leases, manufacturing and service contracts, licenses, royalties, development and collaboration arrangements, and other research and development activities. The following table summarizes our significant binding contractual obligations at June 30, 2019 (in thousands):

	Payments due by period				
	Less than 1 year	1 to 3 years	3 to 5 years	More than 5 years	Total
Operating leases	$ 9,739	$ 15,921	$ 14,007	$ 10,384	$ 50,051
Manufacturing and service contracts	4,788	1,394	—	—	6,182
Total	$ 14,527	$ 17,315	$ 14,007	$ 10,384	$ 56,233

The terms of certain of our licenses, royalties, development and collaboration agreements, as well as other research and development activities, require us to pay potential future milestone payments based on product development success. The above table excludes such obligations as the amount and timing of such obligations are unknown or uncertain.

Off-Balance Sheet Arrangements

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*

Interest Rate 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, 2019, we had cash, cash equivalents, and investments totaling $618.3 million which includes bank deposits, money market funds, U.S. government treasury and agency securities, and investment-grade corporate bond securities 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 change in interest rates during any of the periods presented would not have had a material impact on our consolidated financial statements. To date, we have not experienced a loss of principal on any of our investments.

Foreign Currency Risk

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. For the six months ended June 30, 2019, a majority of our revenue and expense activities and capital expenditures were denominated in U.S. dollars. A hypothetical 10% change in foreign exchange rates during any of the periods presented would not have had a material impact on our consolidated 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 Quarterly Report, pursuant to Rules 13a-15(b) and 15d-15(b) under the Securities Exchange Act of 1934, 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, 2019. 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

There have been no 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, 2019, 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 or government regulators and we may, from time to time, make claims or take legal actions to assert our rights, including claims relating to our directors, officers, stockholders, intellectual property rights, 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 materialize, 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.

The following description of the risk factors associated with our business includes any material changes to and supersedes the description of the risk factors associated with our business previously disclosed in Part I, Item 1A of the Annual Report.

Risks Related to Our Financial Condition and Capital Requirements

We have a history of operating losses and anticipate that we will continue to incur losses for the foreseeable future.

We are a biopharmaceutical company with a history of operating losses, and anticipate continuing to incur operating losses for the foreseeable future. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We have devoted substantially all of our financial resources to identifying, acquiring, and developing our products and product candidates, including conducting clinical studies, developing manufacturing processes, manufacturing product candidates for clinical studies, and providing selling, general and administrative support for these operations. The amount of our future net losses will depend, in part, on non-recurring events, the success of our commercialization efforts, and the rate of our future expenditures. 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 products and product candidates;
- change or add additional manufacturers or suppliers;
- seek to expand upon or build our own manufacturing-related facilities and capabilities;
- seek regulatory and marketing approvals for our product candidates that successfully complete clinical studies;
- continue to establish Medical Affairs field teams to initiate relevant disease education;
- continue to establish a marketing and distribution infrastructure and field force to commercialize our products and any product candidates for which we may obtain marketing approval;
- continue to manage our international subsidiaries and establish new ones;
- continue to operate as a public company and comply with legal, accounting and other regulatory requirements;
- seek to identify, assess, license, acquire, and/or develop other product candidates, technologies, and/or businesses;
- make milestone or other payments under any license or other 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 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.

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 are just starting to generate revenue from product sales.

Our ability to generate significant revenue from product sales depends on our ability, alone or with strategic collaboration partners, to successfully commercialize our products and to complete the development of, and obtain the regulatory and marketing approvals necessary to commercialize, one or more of our product candidates. 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:

- obtaining regulatory and marketing approvals with broad indications for product candidates for which we complete clinical studies;
- developing a sustainable and scalable manufacturing process for our products and 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 market demand for our products and product candidates, if approved;
- launching and commercializing our products and product candidates for which we obtain regulatory and marketing approval, either directly or with a collaborator or distributor;
- obtaining market acceptance of our products and product candidates as viable treatment options;
- obtaining adequate market share, reimbursement and pricing for our products and product candidates;
- our ability to sell our products and product candidates on a named patient basis or through an equivalent mechanism and the amount of revenue generated from such sales;
- our ability to find patients so they can be diagnosed and begin receiving treatment;
- addressing any competing technological and market developments;
- negotiating favorable terms, including commercial rights, in any collaboration, licensing, or other arrangements into which we may enter, any amendments thereto or extensions thereof;
- maintaining, protecting, and expanding our portfolio of intellectual property rights, including patents, trade secrets, and know-how; and
- attracting, hiring, and retaining qualified personnel.

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 our products, even if approved.

We expect we will need to raise additional capital to fund our activities. This additional financing may not be available on acceptable terms, if 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.

As of June 30, 2019, our available cash, cash equivalents, and investments were $618.3 million. We expect we may need additional capital to continue to commercialize our products, and to develop and 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 and commercial supplies of our products and product candidates;
- the cost of creating additional infrastructure, including facilities and systems;
- the number and characteristics of the product candidates that we pursue;
- the cost, timing, and outcomes of regulatory approvals;
- the cost and timing of establishing and operating our international subsidiaries;
- the cost and timing of establishing and operating field forces, marketing, and distribution capabilities;
- the cost and timing of other activities needed to commercialize our products; and
- the terms and timing of any collaborative, licensing, acquisition, and other arrangements that we may establish, including any required milestone, royalty, and reimbursements or 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 our product candidates and commercialize our products. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. 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. If we incur debt, it 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. If we are granted priority review vouchers in connection with regulatory approvals for our product candidates, we may be unable to sell the vouchers or, if we do sell the vouchers, we may have to sell them on unfavorable terms and at prices that are lower than expected. There is no guarantee that we will be granted priority review vouchers in connection with product approvals, and regulatory authorities may cease granting such vouchers in the future. We could also be required to seek funds through collaborative partnerships, strategic alliances, and licensing or other arrangements and we may be required to relinquish rights to some of our technologies or product candidates, future revenue streams, research programs, and other 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 or at all, we may be required to significantly curtail, delay, or discontinue one or more of our research or development programs or the commercialization of our products and any approved 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

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. The safety or efficacy results generated to date in clinical studies do not ensure that later clinical studies will demonstrate similar results. For example, our Phase 3 studies that evaluated Ace-ER in patients with GNE myopathy and UX007 in patients with Glut1 DS experiencing disabling paroxysmal movement disorders did not achieve their primary or secondary endpoints. 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. Given the illness of the patients 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. 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:

- delays or failures in generating 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;
- failure to demonstrate a starting dose for our product candidates in the clinic that might be reasonably expected to result in a clinical benefit;
- delays or failures in developing gene therapy, messenger RNA (mRNA), DNA, small interfering RNA (siRNA) or other novel and complex product candidates, which are expensive and difficult to develop and manufacture;
- delays resulting from a shutdown, or uncertainty surrounding the potential for future shutdowns of the U.S. government, including the FDA;
- delays or failures in reaching a consensus with regulatory agencies on study design;

- delays in reaching agreement on acceptable terms with contract research organizations, or CROs, clinical study sites, and other clinical trial-related vendors;
- failure or delays in obtaining required regulatory agency approval and/or IRB or EC approval at each clinical study site or in certain countries;
- failure to correctly design clinical studies which may result in those studies failing to meet their endpoints or the expectations of regulatory agencies;
- changes in clinical study design or development strategy resulting in delays related to obtaining approvals from IRBs or ECs and/or regulatory agencies to proceed with clinical studies;
- 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 and/or ICH'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;
- adverse events associated with the product candidate occurring that are viewed to outweigh its potential benefits;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;
- greater than anticipated costs associated with clinical studies of our drug candidates;
- 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, we may need to conduct additional toxicology, comparability or other studies to bridge our modified product candidates to earlier versions. Clinical study delays could also shorten any periods during which our products have commercial exclusivity 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.

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 timing of patient dosing, the submission or acceptance 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 from our estimates. If we do not meet these publicly announced milestones, 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.

We may find it difficult to identify and 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 hundred patients in the United States suffer from TIO, for which Crysvita 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 approximately 8,000 patients in the developed world suffer from late-onset OTC deficiency, for which DTX301 is being studied, and these all may not be treatable if they are immune to the virus; and
- we estimate that approximately 6,000 patients worldwide suffer from GSD1a, for which DTX401 is being studied, and these all may not be treatable if they are immune to the virus.

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 patients to 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. The process of finding and diagnosing patients may prove costly, especially since the rare diseases we are studying are commonly under diagnosed. We also may not be able to identify, recruit, and enroll a sufficient number of appropriate patients to complete our clinical studies because of demographic criteria for prospective patients, 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. 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. Furthermore, 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. 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.

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 commercialize our products and 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. We have only obtained regulatory approval for two products, 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 be denied. 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:

- regulatory authorities may disagree with the design, implementation, or conduct of our clinical studies;
- 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;
- 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;
- we may be unable to demonstrate to regulatory authorities that a product candidate's risk-benefit ratio for its proposed indication is acceptable;
- regulatory authorities may fail to approve the manufacturing processes, test procedures and specifications, or facilities used to manufacture our clinical and commercial supplies;

- the U.S. government may be shut down, which could delay the FDA;
- failure of our nonclinical or clinical development to comply with an agreed upon Pediatric Investigational Plan (PIP), which details the designs and completion timelines for nonclinical and clinical studies and is a condition of marketing authorization in the EU; and
- the approval policies or regulations of 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. Additionally, many of the disease states we are targeting, such as LC-FAOD, are highly heterogeneous in nature, which may impact our ability to determine the treatment benefit of our potential therapies.

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

The regulatory approval process for novel product candidates, such as our gene therapy product candidates, can be more expensive and take longer than for other product candidates, and may change in the future.

The clinical trial requirements of regulatory authorities and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the product candidate. As a result, the regulatory approval process for novel product candidates such as our gene therapy product candidates can be more expensive and take longer than for other, better known or more extensively studied product candidates, which can lead to fewer product approvals. To date, very few gene therapy products have received regulatory approval in the United States or Europe.

Additionally, the FDA, Health Canada, and the EMA have each expressed interest in further regulating biotechnology, including gene therapy and genetic testing. For example, the EMA, which governs the development of gene therapies in the EU and may issue new guidelines concerning the development and marketing authorization for gene therapy products, advocates a risk-based approach to the development of a gene therapy product. Agencies at both the federal and state level in the United States, as well as U.S. congressional committees and foreign governments, have also expressed interest in further regulating the biotechnology industry. Different regulatory approaches by jurisdiction can result in different or additional preclinical studies or clinical trials being required to support regulatory approval in each jurisdiction.

Regulatory requirements such as review committees and advisory groups, the new guidelines they promulgate, and new guidance issued by regulatory authorities may lengthen the regulatory review process, require us to perform additional studies or trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our product candidates or lead to significant post- approval limitations or restrictions. As we advance our product candidates, we will be required to consult with these regulatory and advisory groups and comply with applicable guidelines. If we fail to do so, we may be required to delay or discontinue development of such product candidates. These additional processes may result in a review and approval process that is longer than we otherwise would have expected. Delays as a result of an increased or lengthier regulatory approval process or further restrictions on the development of our product candidates can be costly and could negatively impact our or our collaborators' ability to complete clinical trials and commercialize our current and future product candidates in a timely manner, if at all.

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, the delay or denial of regulatory approval by the FDA or other comparable foreign authorities, or 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. Our product candidates are in development and the safety profile has not been established. For example, in a completed Phase 2 study, LC-FAOD patients treated with UX007 experienced treatment-related adverse events, the most common of which were diarrhea, abdominal/gastrointestinal pain and vomiting. There was one treatment-related serious adverse event of moderate gastroenteritis with vomiting. There were two deaths during the LC-FAOD extension study, both deemed to be related to disease progression and not due to treatment with UX007. Gene therapy product candidates using AAV vectors, like DTX301, have been associated with immunologic reaction to the capsid protein or gene at early time points after administration. For example, in our discontinued Phase 1/2 clinical trial of DTX101 in hemophilia B, we observed elevated laboratory alanine transaminase levels, or ALTs. In previous clinical trials involving AAV viral vectors for gene therapy, some subjects experienced adverse events, including the development of a T-cell mediated immune response against the vector capsid proteins. In addition, theoretical side effects of AAV vectors include replication and spread of the virus to other parts of the body and insertional oncogenesis, which is the process whereby the insertion of a gene near a gene that is important in cell growth or division results in uncontrolled cell division, which could potentially enhance the risk of malignant transformation or cancer. Potential procedure-related events are similar to those associated with standard coronary diagnostic procedures, and may include vascular injury (e.g., damage to the femoral, radial or brachial arteries at the site of vascular access, or damage to the coronary arteries) or myocardial injury. Future product candidates may also cause these or similar side effects as 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 a 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, even though we received regulatory approval for Crysvita and Mepsevii and even if our product candidates receive marketing approval in the future, if 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 REMS plan;
- 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.

Serious adverse events in clinical trials involving gene therapy product candidates may damage public perception of the safety of our product candidates, increase government regulation, and adversely affect our ability to obtain regulatory approvals for our product candidates or conduct our business.

Gene therapy remains a novel technology. Public perception may be influenced by claims that gene therapy is unsafe, and gene therapy may not gain the acceptance of the public or the medical community. For example, earlier gene therapy trials using other vectors led to several well- publicized adverse events, including cases of leukemia and death. The risk of cancer remains a concern for gene therapy and we cannot assure you that it will not occur in any of our planned or future clinical studies. In addition, there is the potential risk of delayed adverse events following exposure to gene therapy products due to persistent biological activity of the genetic material or other components of products used to carry the genetic material. Serious adverse events in our clinical trials, or other

clinical trials involving gene therapy products, particularly AAV gene therapy products such as candidates based on the same capsid serotypes as our product candidates, or occurring during use of our competitors' products, even if not ultimately attributable to the relevant product candidates, and the resulting publicity, could result in increased government regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our gene therapy product candidates, stricter labeling requirements for those gene therapy product candidates that are approved and a decrease in demand for any such gene therapy product candidates, all of which would have an adverse effect on our business, financial condition, results of operations and prospects.

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

Our products and any product candidates that are approved 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 4 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 was 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 promote our products only for indications or uses for which they 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.

If we are unable to identify, source, and develop effective predictive biomarkers, or our collaborators are unable to successfully develop and commercialize companion diagnostics for our product candidates, or experience significant delays in doing so, we may not realize the full commercial potential of our product candidates.

We are developing companion diagnostic tests to identify the right patients for certain of our product candidates and to monitor response to treatment. In certain cases, diagnostic tests may need to be developed as companion diagnostics and regulatory approval obtained in order to commercialize some product candidates. We expect to use predictive biomarkers to identify the right patients for certain of our product candidates. For example, to evaluate therapeutic response of DTX301, we are measuring ammonia levels and

other biomarkers, including ^{13}C-acetate, which are established measures of OTC deficiency disease status and ureagenesis. We cannot assure you that ^{13}C-acetate or any other future potential biomarker will in fact prove predictive, be reliably sourced, or be accepted by the FDA or other regulatory authorities. In addition, our success may depend, in part, on the development and commercialization of companion diagnostics. We also expect the FDA will require the development and regulatory approval of a companion diagnostic assay as a condition to approval of DTX301. There has been limited success to date industrywide in developing and commercializing these types of companion diagnostics. Development and manufacturing of companion diagnostics is complex and there are limited manufacturers with the necessary expertise and capability. Even if we are able to find a qualified collaborator, it may not be able to manufacture the companion diagnostics at a cost or in quantities or on timelines necessary for use with our product candidates. To be successful, we need to address a number of scientific, technical and logistical challenges. We have not yet initiated development and commercialization of companion diagnostics. We have little experience in the development and commercialization of diagnostics and may not be successful in developing and commercializing appropriate diagnostics to pair with any of our product candidates that receive marketing approval. University of Pennsylvania School of Medicine currently conducts some of our clinical assays pursuant to a sponsored research agreement, one of which is required for our ongoing Phase 1/2 clinical trial. We intend to enter into agreements with third parties for the automation, characterization and validation, of our companion diagnostic and the manufacture of its critical reagents. However, we may be unable to enter into any such agreement on favorable terms, or at all.

Companion diagnostics are subject to regulation by FDA and similar regulatory authorities outside the United States as medical devices and require regulatory clearance or approval prior to commercialization. In the United States, companion diagnostics are cleared or approved through FDA's 510(k) premarket notification or premarket approval, or PMA, process. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted 510(k) premarket notification, PMA or equivalent application types in jurisdictions outside the United States, may cause delays in the approval, clearance or rejection of an application. Given our limited experience in developing and commercializing diagnostics, we expect to rely in part or in whole on third parties for companion diagnostic design and commercialization. We and our collaborators may encounter difficulties in developing and obtaining approval or clearance for the companion diagnostics, including issues relating to selectivity/specificity, analytical validation, reproducibility, or clinical validation. Any delay or failure by us or our collaborators to develop or obtain regulatory approval of the companion diagnostics could delay or prevent approval of our product candidates.

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, collaborative partners, and independent investigators 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 mRNA, DNA and siRNA collaborations. 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, GCP, and 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 efforts to support patient diagnosis and identify patients, 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 KKC for the clinical and commercial supply of Crysvita for all major markets and for the development and commercialization of Crysvita in certain major markets, and KKC's failure to provide an adequate supply of Crysvita or to commercialize Crysvita in those markets could result in a material adverse effect on our business and operating results.

Under our agreement with KKC, KKC has the sole right to commercialize Crysvita in Europe and, at a specified time, in the United States, Canada, and Turkey, subject to a limited promotion right we retained. Our development partnership with KKC 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:

- KKC has no obligation under our agreement to use diligent efforts to commercialize Crysvita 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 Crysvita by KKC in Europe.
- the timing and amount of any royalty payments we may receive under our agreement with KKC will depend on, among other things, the efforts, allocation of resources, and successful commercialization of Crysvita by KKC in the United States and Canada under our agreement;
- KKC may change the focus of its commercialization efforts or pursue higher-priority programs;
- KKC may make decisions regarding the indications for our product candidates in countries where it has the sole right to commercialize the product candidates that limit commercialization efforts in those countries or in countries where we have the right to commercialize our product candidates;
- KKC may make decisions regarding market access and pricing in countries where it has the sole right to commercialize our product candidates which can negatively impact our commercialization efforts in countries where we have the right to commercialize our product candidates;
- KKC may fail to manufacture or supply sufficient drug product of Crysvita in compliance with applicable laws and regulations or otherwise for our development and clinical use, which could result in program delays;
- KKC may fail to manufacture or supply sufficient drug product of Crysvita in compliance with applicable laws and regulations or otherwise for our commercial use, which could result in lost revenue;
- KKC may elect to develop and commercialize Crysvita indications with a larger market than XLH and at a lower price, thereby reducing the profit margin on sales of Crysvita for any orphan indications, including XLH;
- if KKC were to breach or terminate the agreement with us, we would no longer have any rights to develop or commercialize Crysvita or such rights would be limited to non-terminated countries;
- KKC 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 KKC may be greater than anticipated.

We rely on third parties to manufacture our products and most of 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 cost.

We have limited infrastructure or capability internally to manufacture our products and product candidates, and we lack the resources and the capability to manufacture most 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 products and 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 a 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 have no experience as a company developing a manufacturing facility and may not be able to do so successfully if we determine to expand or develop our manufacturing capability and infrastructure.

We expect our future manufacturing strategy to involve the use of one or more CMOs as well as our own capabilities and infrastructure, including at our Woburn, MA facility or new facilities we may develop. We expect that development of our own process development facility will provide us with enhanced control of material supply for both clinical trials and the commercial market, enable the more rapid implementation of process changes, and allow for better long-term margins. However, we have no experience as a company in developing a manufacturing facility and may never be successful in developing our own manufacturing facility or capability. Additionally, given that cGMP gene therapy manufacturing is a nascent industry, there are a small number of CMOs with the experience necessary to manufacture our gene therapy product candidates and we may have difficulty finding or maintaining relationships with such CMOs or hiring experts for internal manufacturing and accordingly, our production capacity may be limited. We may establish multiple manufacturing facilities as we expand our commercial footprint to multiple geographies, which may lead to regulatory delays or prove costly. Even if we are successful, our manufacturing capabilities could be affected by cost-overruns, unexpected delays, equipment failures, lack of capacity, labor shortages, natural disasters, power failures, program failures, and numerous other factors that could prevent us from realizing the intended benefits of our manufacturing strategy and have a material adverse effect on our business.

Gene therapy and mRNA, DNA and siRNA product candidates are novel, complex, expensive and difficult to manufacture. We could experience manufacturing problems that result in delays in developing and commercializing these programs or otherwise harm our business.

The manufacturing process used to produce our gene therapy, mRNA, DNA and siRNA product candidates is novel, complex, and has not been validated for commercial use. Several factors could cause production interruptions, including equipment malfunctions, regulatory inspections, facility contamination, raw material shortages or contamination, natural disasters, disruption in utility services, human error or disruptions in the operations of our suppliers.

Our gene therapy, mRNA, DNA and siRNA product candidates require processing steps that are more complex than those required for most small molecule drugs. Moreover, unlike small molecules, the physical and chemical properties of a biologic such as gene therapy, mRNA, DNA and siRNA product candidates generally cannot be fully characterized. As a result, assays of the finished product candidate may not be sufficient to ensure that the product candidate is consistent from lot to lot or will perform in the intended manner. Accordingly, we employ multiple steps to control the manufacturing process to assure that the process works reproducibly and the product candidate is made strictly and consistently in compliance with the process. Problems with the manufacturing process, even minor deviations from the normal process, could result in product defects or manufacturing failures that result in lot failures, noncompliance with regulatory requirements, product recalls, product liability claims or insufficient inventory. We may encounter problems achieving adequate quantities and quality of clinical-grade materials that meet FDA, the EMA or other applicable standards or specifications with consistent and acceptable production yields and costs.

In addition, FDA, the EMA and other foreign regulatory authorities may require us to submit samples of any lot of any approved product together with the protocols showing the results of applicable tests at any time. Under some circumstances, FDA, the EMA or other foreign regulatory authorities may require that we not distribute a lot until the agency authorizes its release. Slight deviations in the manufacturing process, including those affecting quality attributes and stability, may result in unacceptable changes in the product that could result in lot failures or product recalls. Lot failures or product recalls could cause us to delay product launches or clinical trials, which could be costly to us and otherwise harm our business, financial condition, results of operations and prospects.

We also may encounter problems hiring and retaining the experienced scientific, quality-control and manufacturing personnel needed to operate the manufacturing processes for our gene therapy, mRNA, DNA and siRNA product candidates, which could result in delays in production or difficulties in maintaining compliance with applicable regulatory requirements. We may be unable to scale

up existing or new facilities, including our facility in Woburn, MA, and such facilities may not enable the expansion of our internal manufacturing process discovery and development to the extent we anticipate, or at all.

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

The process of manufacturing our products and product candidates is complex, highly regulated, and subject to several risks, including but not limited to those listed below.

- The process of manufacturing our products and 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 our products and 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 products and product candidates or in the manufacturing facilities in which our products and product candidates are made, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination.
- The manufacturing facilities in which our products and 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 products and product candidates may result in shipment delays, inventory shortages, lot failures, withdrawals or recalls, or other interruptions in the supply of our products and 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 products and product candidates. We may also have to take inventory write-offs and incur other charges and expenses for products and product candidates that fail to meet specifications, undertake costly remediation efforts, or seek more costly manufacturing alternatives.

The drug substance and drug product for our products and 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.

We acquire most of the drug substances and drug products for our products and product candidates from single sources. The drug substance and drug product for Crysvita are made by KKC pursuant to our license and collaboration agreement with KKC. The drug substance and drug product for Mepsevii are manufactured by Rentschler under a commercial supply and services agreement and accompanying purchase orders. The pharmaceutical-grade drug substance for UX007 is manufactured by IOI Oleo 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. Single source suppliers are also used for our gene therapy programs. We have not currently secured any other suppliers for the drug substance or drug product of our products and 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 commercialization of our products or 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 commercialization of our products or 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 and collaboration partners 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 products and 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 cannot schedule manufacturing to meet inspectional demands or 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, such as KKC, 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, our collaborators, or third parties with whom we contract could materially harm our business.

If we, our collaborators, including KKC, 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.

The actions of distributors could affect our ability to sell or market products profitably. Fluctuations in buying or distribution patterns by such distributors could adversely affect our revenues, financial condition, or results of operations.

We intend to rely on commercial distributors for a considerable portion of our product sales and we expect such sales to be concentrated within a small number of distributors. The financial failure of any of these distributors could adversely affect our revenues, financial condition or results of operations. Our revenues, financial condition or results of operations may also be affected by fluctuations in distributor buying or distribution patterns. These fluctuations may result from seasonality, pricing, wholesaler inventory objectives, or other factors.

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 in connection with the development and manufacture of our products and product candidates and will likely rely on third parties in connection with the commercialization of our approved products, 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 Products and Product Candidates

If the market opportunities for our products and 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 products and 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 that may reduce the penetration of Crysvita 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 products and 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 products and 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 products and product candidates may be limited or may not be amenable to treatment with our products and product candidates, and new patients may become increasingly difficult to identify or access, which would adversely affect our results of operations and our business. Further, even if we obtain significant market share for our products and 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.

Manufacturers that produce our products and product candidates may not have experience producing our products and product candidates at commercial levels and may not achieve the necessary regulatory approvals or produce our products and product candidates at the cost, quality, quantities, locations, and timing needed to support profitable commercialization.

We rely on third-party manufacturers to produce our products and product candidates. These manufacturers may not have the experience or ability to produce our products and 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 for all of our product candidates. If our manufacturing partners are not able to conduct all such necessary activities in accordance with applicable regulations, our commercialization efforts will be harmed. We have not yet secured manufacturing capabilities for commercial quantities of all of our product candidates and may be unable to negotiate binding agreements with manufacturers to support our commercialization activities on commercially reasonable terms.

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 products and product candidates, are unable to comply with GMP or other pertinent regulatory requirements, or are unable to produce our products and product candidates within our planned timeframe and cost parameters, the development and sales of our products and product candidates, if approved, may be materially harmed.

Additionally, the cost to us for the supply of our products and 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 products and product candidates in a compliant and timely manner. Furthermore, KKC is our sole supplier of commercial quantities of Crysvita. The supply price to us for commercial sales of Crysvita, which is determined on a fixed double-digit percentage of net sales, is 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 treatments that may compete with our products and product candidates. For example, XLH is treated with oral phosphate and vitamin D therapy, which may compete with Crysvita; LC-FAOD is managed with diet therapy and medium-chain triglyceride oil, which may compete with UX007; OTC deficiency is currently treated with nitrogen scavenging drugs and severe limitations in dietary protein, which may compete with DTX301; and GSD1a is currently treated with corn starch, which may compete with DTX401. Triheptanoin is available in food-grade form, which may compete with our pharmaceutical-grade product. Furthermore, investigator-sponsored trials evaluating triheptanoin in multiple indications are ongoing. 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, biotechnology companies, startups, academic research institutions, government agencies, and public and private research institutions. 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 products and product candidates uneconomical or obsolete, and we may not be successful in marketing our products and product candidates against competitors.

We continue to build and evolve an integrated commercial organization. If we are unable to expand our existing commercial infrastructure or enter into agreements with third parties to market and sell our product candidates, as needed, we may be unable to generate significant revenue.

In preparation to successfully commercialize Crysvita and Mepsevii as well as any additional products that may result from our development programs, we are building a commercial infrastructure in North America, Europe and Latin America. This infrastructure consists of both office based as well as field teams with technical expertise, and will be expanded as we approach the potential approval dates of additional products that result from our development programs. This will be expensive and time consuming. Any failure or delay in the expansion of this infrastructure may adversely impact the commercialization of our approved products.

Although our employees may have promoted other similar products in the past while employed at other companies, we, as a company, have limited, recent experience selling and marketing our product. Further, given our limited 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 a large 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 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 current and future products will depend in part on the medical community, patients, and payors accepting our current and future products 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 current and future products 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 current and future products 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 products and 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. We expect the cost of a single administration of gene therapy products, such as those we are developing, to be substantial, when and if they achieve regulatory approval. Accordingly, the availability and adequacy of coverage and reimbursement by governmental and private payors are essential for most patients to afford expensive treatments such as ours, assuming approval. Sales of our products and product candidates, if approved, will depend substantially, both domestically and abroad, on the extent to which their costs 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, are available only to limited levels, or are not available on a timely basis, we may not be able to successfully commercialize our products and product candidates, if approved. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to sustain our overall enterprise.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, 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 or private payors will decide with respect to reimbursement for products such as ours, especially our gene therapy product candidates as there is a limited body of established practices and precedents for gene therapy products.

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 products and 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 and, as a result, they may not cover or provide adequate payment for our products and product candidates. We expect to experience pricing pressures in connection with the sale of any of our products and product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, additional legislative changes, and statements by elected officials. For example, proposals are being discussed to tie U.S. drug prices to the cost in other countries, 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.

The results of the United Kingdom's referendum on withdrawal from the EU may have a negative effect on our business, global economic conditions, and financial markets.

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the EU, commonly referred to as Brexit. On March 29, 2017, the country formally notified the EU of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. Since a significant proportion of the regulatory framework in the United Kingdom is derived from EU directives and regulations, Brexit could materially impact the regulatory regime with respect to the approval of product candidates, disrupt the manufacture of our products and product candidates in the United Kingdom or the EU, disrupt the importation and export of active substances and other components of drug formulations, and disrupt the supply chain for clinical trial product and final authorized formulations. Any delay in obtaining, or an inability to obtain, any marketing approvals, or disruption to our and our collaborators' supply chain as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the United Kingdom and/or the EU and restrict our ability to generate revenue and achieve and sustain profitability. The cumulative effect of disruptions to the regulatory framework or supply chains may add considerably to the development lead time to, and expense of, marketing authorization and commercialization of products in the EU and/or the United Kingdom. In view of the uncertainty surrounding the Brexit implementation, we are unable to predict the effects of such disruption to the regulatory framework and supply chain in Europe.

Further, these developments, or the perception that any of them could occur, have had and may continue to have a material adverse effect on global economic conditions and the stability of global financial markets, and could significantly reduce global market liquidity and restrict the ability of key market participants to operate in certain financial markets. Asset valuations, currency exchange rates and credit ratings may be especially subject to increased market volatility. Lack of clarity about future U.K. laws and regulations as the United Kingdom determines which EU laws to replace or replicate in the event of a withdrawal, including financial laws and regulations, tax and free trade agreements, intellectual property rights, supply chain logistics, environmental, health and safety laws and regulations, immigration laws and employment laws, could decrease foreign direct investment in the United Kingdom, increase costs and depress economic activity. If the United Kingdom and the EU are unable to negotiate and obtain the necessary government approvals for acceptable withdrawal terms or if other EU member states pursue withdrawal, barrier-free access between the United Kingdom and other EU member states or among the European economic area overall could be diminished or eliminated. In addition, we expect that Brexit could lead to legal uncertainty and potentially divergent national laws and regulations as the United Kingdom determines which EU laws to replicate or replace. We are taking certain precautionary measures with respect to Brexit and its impact to the EU, and will continue to monitor the situation. If the United Kingdom were to significantly alter its regulations affecting the biotechnology or pharmaceutical industries, we could face significant new costs. It may also be time-consuming and expensive for us to alter our internal operations in order to comply with new regulations. Any of these factors could have a material adverse effect on our business, financial condition and results of operations and affect our strategy in the U.K. and EU biotech market.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain effective patent rights for our products, 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, our products, and our 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, our products, and our product candidates.

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 products or 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 products or 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 the patents and patent applications we own or in-license are unchallenged, they may not adequately protect our intellectual property, provide exclusivity for our products or 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 products or 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 products and product candidates in all territories. For example, there are no issued patents covering the Crysvita composition of matter in Latin America where we have rights to commercialize the compound. Therefore, a competitor could develop the same antibody or a similar antibody as well as other approaches that target FGF23 for potential commercialization in Latin America, subject to any intellectual property rights or regulatory exclusivities awarded to us. If we cannot obtain and maintain effective patent rights for our products or 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 its effective filing date. 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 Crysvita, Mepsevii, UX007, DTX301, and DTX401, we cannot provide any assurances that any such patent term extension will be obtained and, if so, for how long. Furthermore, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than we request. If we do not have sufficient patent terms or regulatory exclusivity to protect our products, our business and results of operations may 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 16, 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 also 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 courts have only begun to address these provisions. 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 products, 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 products or 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, *inter partes* reviews, post grant reviews, 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 products or 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 products or product candidates. We have conducted freedom to operate analyses with respect only to our products and 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 products or 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 products or product candidates may infringe.

We are aware of three third-party patent families that include issued U.S. patents with claims that, if valid and enforceable, could be construed to cover one or more of our gene therapy product candidates, if and when approved, or methods of their manufacture. We are also aware of an additional three third-party patent families that include issued European claims that, if valid and enforceable, could be construed to cover certain methods that may be used in the manufacture of one or more of our gene therapy product candidates. 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 our products or 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 our products or a 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 continue commercialization of our products, or block our ability to 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 commercialize 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 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 Crysvita, Mepsevii, DTX301, and DTX401.

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 Crysvita, Mepsevii, DTX301, and DTX401. In the United States, the Biologics Price Competition and Innovation Act of 2009, or BPCI Act, was included in the Affordable Care Act and 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. Moreover, it is not known whether the BPCI Act will survive in whole or in part if the Affordable Care Act is repealed by Congress or held unconstitutional by courts. As a result, its ultimate impact, implementation, meaning, and long-term existence are subject to uncertainty. Elimination or modification of the BPCI Act, or changes to the FDA's interpretation or implementation of the BPCI Act, could have a material adverse effect on the future commercial prospects for Crysvita, Mepsevii, DTX301, and DTX401.

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 or future small-molecule product candidates.

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, and 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 enforce its patents, approval of the ANDA is stayed for 30 months, or as lengthened or shortened by the court.

Accordingly, if UX007 is approved, competitors could file ANDAs for generic versions of UX007, or 505(b)(2) NDAs that reference UX007. If there are patents listed for UX007 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 KKC, who is primarily responsible for the prosecution of patents and patent applications licensed to us under the collaboration agreement.

In addition, we have in-licensed patents and patent applications owned by the University of Pennsylvania, relating to the AAV8 vector used in DTX301 and DTX401. These patents and patent applications are licensed or sublicensed by REGENXBIO and sublicensed to us. We do not have the right to control the prosecution of these patent applications, or the maintenance of any of these patents. In addition, under our agreement with REGENXBIO, we do not have the first right to enforce the licensed patents, and our enforcement rights are subject to certain limitations that may adversely impact our ability to use the licensed patents to exclude others from commercializing competitive products. Moreover, REGENXBIO and the University of Pennsylvania may have interests which differ from ours in determining whether and the manner in which to enforce such patents.

If KKC, the University of Pennsylvania, or any of our future licensing partners fail to appropriately prosecute, maintain, and enforce patent protection for the 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 and Collaboration Agreements" in the Annual Report for a description of our license agreements with KKC, Baylor Research Institute, Saint Louis University, Bayer, REGENXBIO, and the University of Pennsylvania, which include descriptions of the termination provisions of these agreements.

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 intellectual property 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 intellectual property litigation, if we or one of our licensing partners were to initiate legal proceedings against a third party to enforce a patent covering our products or one of our product candidates, the defendant could counterclaim that the patent covering our product or 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 or derivation proceedings now available under the Leahy-Smith Act provoked by third parties or brought by us or declared or instituted 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. In addition, the validity of our patents could be challenged in the USPTO by one of the new post grant proceedings (*i.e., inter partes* review or post grant review) now available under the Leahy-Smith Act. Our defense of litigation, interference proceedings, or post grant proceedings under the Leahy-Smith Act 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 distract 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 to successfully defend against 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 distract 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 biotechnology and pharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology and pharmaceutical industries involves both technological and legal complexity. Therefore, obtaining and enforcing such 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. For example, in *Association for Molecular Pathology v. Myriad Genetics, Inc.*, the Supreme Court ruled that a "naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated," invalidating Myriad Genetics' patents on the BRCA1 and BRCA2 genes. Certain claims of our licensed U.S. patents covering DTX301 and DTX401 relate to isolated AAV8 vectors, capsid proteins, or nucleic acids. To the extent that such claims are deemed to be directed to natural products, or to lack an inventive concept above and beyond an isolated natural product, a court may decide the claims are invalid under *Myriad*. Additionally, there have been recent proposals for additional changes to the patent laws of the United States and other countries that, if adopted, could impact our ability to obtain patent protection for our proprietary technology or our ability to enforce our proprietary technology. Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO and the relevant law-making bodies in other countries, 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 our products or 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 KKC 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. 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 and for various subtypes of LC-FAOD in Europe, as well as for Crysvita, Mepsevii, DTX301 and DTX401 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 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.

Our operating results would be adversely impacted if our intangible assets become impaired.

As a result of the accounting for our acquisition of Dimension Therapeutics, Inc. (Dimension) in November 2017, we have recorded on our balance sheet intangible assets for in-process research and development ("IPR&D") and an acquired contract asset. We test the intangible assets for impairment annually during the fourth quarter and more frequently if events or changes in circumstances indicate that it is more likely than not that the asset is impaired. If the associated research and development effort is abandoned, the related assets will be written-off and we will record a noncash impairment loss on our statement of operations. We have not recorded any impairments related to our intangible assets through the end of June 30, 2019.

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, require 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.

If we are unable to maintain and further develop effective internal control over financial reporting, investors may lose confidence in the accuracy and completeness of our financial reports and the market price of our stock may decrease.

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 also subject to the compliance requirements of Section 404(b) of the Sarbanes-Oxley Act, which results in us incurring substantial expenses and expending significant management efforts. We currently do not have a separate internal audit group. We may 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 or our independent registered public accounting firm identify deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses, investors may lose confidence in the accuracy and completeness of our financial reports, 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, the Affordable Care Act, as amended, substantially changed the way health care is financed by both governmental and private insurers, and significantly impacts the U.S. pharmaceutical industry. The Affordable Care Act, 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, and establishes annual fees and taxes on manufacturers of certain branded prescription drugs. A federal district court ruled the entire Affordable Care Act to be unconstitutional in December 2018, but issued a stay, meaning the law will remain in effect while the ruling is appealed. Implementation of the Affordable Care Act remains ongoing, but there is uncertainty as to how the law's various provisions will ultimately affect the industry and whether the law will remain in place.

Other legislative changes have been adopted in the United States, including the Cures Act and the Budget Control Act of 2011, or the Budget Act, signed into law on August 2, 2011. The Cures Act introduced a wide range of reforms and the Budget Act, 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. In 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 has been extended to 2025.

We expect that additional state and federal healthcare reform measures and regulations will be adopted in the future, including proposals to reduce the exclusivity protections provided to already approved biological products and to provide biosimilar and interchangeable biologic products an easier path to approval. Any of these measures and regulations could limit the amounts that federal and state governments will pay for healthcare products and services, result in reduced demand for our product candidates or additional pricing pressures and affect our product development, testing, marketing approvals and post-market activities.

EU

In the EU, the European Commission has adopted detailed rules for the safety features appearing on the packaging of medicinal products for human use. The regulations set forth 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 at the adoption of notices and guidelines which will serve the interpretation of currently applicable regulations and directives. For example, between August 2015 and December 2016, the European Commission launched public consultations which concerned good manufacturing practices, clinical trials for human medicinal products, and orphan medicinal products. The purpose of the consultation on orphan medicinal products (which will be replaced with a Notice) is to streamline the regulatory framework and to adapt the applicable regulations 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 are subject, directly and 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.

Our operations are directly, and 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 impact, among other things, our field marketing and education programs. In addition, we are 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 are described under "Business—Government Regulation" in the Annual Report. 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. 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.

Our business strategy includes international expansion. 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 and data regulations, transparency regulations, tax laws, export and import restrictions, employment laws, regulatory requirements, and other governmental approvals, permits, and licenses;
- introduction 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 for, 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, results of certain elections and votes, outbreak of disease, boycotts, adoption or expansion of government trade restrictions, 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, including those under the U.K. Bribery Act and similar foreign laws and regulations; 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 have a multinational tax structure and are subject to income tax in the United States and various foreign jurisdictions. Our effective tax rate is influenced by many factors including changes in our operating structure, changes in the mix of our earnings among countries, our allocation of profits and losses among our subsidiaries, our intercompany transfer pricing agreements and rules relating to transfer pricing, the availability of U.S. research and development tax credits, and future changes in tax laws and regulations in the U.S. and foreign countries. Significant judgment is required in determining our tax liabilities including management's judgment for uncertain tax positions. The Internal Revenue Service, other domestic taxing authorities, or foreign taxing authorities may disagree with our interpretation of tax laws as applied to our operations. Our reported effective tax rate and after-tax cash flows may be materially and adversely affected by tax assessments in excess of amounts accrued for our financial statements. This could materially increase our future effective tax rate thereby reducing net income and adversely impacting our results of operations for future periods.

Failure to comply with laws and regulations could harm our business and our reputation.

Our business is subject to regulation by various federal, state, local and foreign governmental agencies, including agencies responsible for monitoring and enforcing employment and labor laws, workplace safety, and tax laws and regulations. In certain jurisdictions, these regulatory requirements may be more stringent than those in the United States, and in other circumstances these requirements may be more stringent in the United States. Noncompliance with applicable regulations or requirements could subject us to investigations, sanctions, mandatory recalls, enforcement actions, disgorgement of profits, fines, damages, civil and criminal penalties, or injunctions. If any governmental sanctions, fines or penalties are imposed, or if we do not prevail in any possible civil or criminal litigation, our business, operating results, financial condition and our reputation could be harmed. In addition, responding to any action will likely result in a significant diversion of management's attention and resources and an increase in professional fees. Enforcement actions and sanctions could further harm our business, operating results, financial condition, and our reputation.

In particular, our research and development activities and our 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, such as viruses, and other hazardous compounds, which subjects us to laws and regulations governing such activities. 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. We cannot guarantee that the safety procedures utilized by us and our third-party manufacturers for handling and disposing of these materials comply with the standards prescribed by these laws and regulations, 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 multiple years 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, 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 CROs 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 a system failure or security breach occurs and interrupts 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, loss of trade secrets or inappropriate disclosure of confidential or proprietary information, including protected health information or personal data of employees or former employees, access to our clinical data, or disruption of the manufacturing process, 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 reputation 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 one of our laboratories are located in the San Francisco Bay Area, and our collaboration partner for Crysvita, KKC, 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 may be inadequate 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.

We may acquire companies or products or engage in strategic transactions, which could divert our management's attention and cause us to incur various costs and expenses.

We may acquire or invest in businesses or products that we believe could complement or expand our business or otherwise offer growth opportunities. For example, we acquired Dimension in November 2017. The pursuit of potential acquisitions or investments may divert the attention of management and may cause us to incur various costs and expenses in identifying, investigating, and pursuing them, whether or not they are consummated. We may not be able to identify desirable acquisitions or investments or be successful in completing or realizing anticipated benefits from such transactions.

In addition, we may receive inquiries relating to potential strategic transactions, including collaborations, licenses, and acquisitions. Such potential transactions may divert the attention of management and may cause us to incur various costs and expenses in investigating and evaluating such transactions, whether or not they are consummated.

Litigation may substantially increase our costs and harm our business.

We have been, and may in the future become, party to lawsuits including, without limitation, actions and proceedings in the ordinary course of business relating to our directors, officers, stockholders, intellectual property, and employment matters, which will cause us to incur legal fees and other costs related thereto, including potential expenses for the reimbursement of legal fees of officers and directors under indemnification obligations. The expense of defending against such litigation may be significant and there can be no assurance that we will be successful in any defense. Further, the amount of time that may be required to resolve such lawsuits is unpredictable, and these actions may divert management's attention from the day-to-day operations of our business, which could adversely affect our business, results of operations, and cash flows. Litigation is subject to inherent uncertainties, and an adverse result in such matters that may arise from time to time could have a material adverse effect on our business, results of operations, and financial condition.

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 products and product candidates;
- decisions by our collaboration partners with respect to the indications for our products and product candidates in countries where they have the right to commercialize the products and product candidates;
- decisions by our collaboration partners regarding market access and pricing in countries where they have the right to commercialize our products and product candidates;
- failure to successfully develop and commercialize our products and 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 products and 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 or our company by the public, legislatures, regulators, and the investment community;
- the perception of the pharmaceutical industry's approach to drug pricing;
- announcements of significant acquisitions, strategic partnerships, joint ventures, or capital commitments by us, our strategic collaboration partners, or our competitors;
- the integration and performance of any businesses we have acquired or may acquire;
- 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. At June 30, 2019, 2,582,049 shares were available for future grants under the 2014 Plan. The number of shares available for future grant under the 2014 Plan will automatically increase on January 1 of each year 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.

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. At June 30, 2019, 2,740,058 shares were available for issuance under the 2014 ESPP. The number of shares available for issuance under the 2014 ESPP will automatically increase on January 1 of each year 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.

Currently we plan to register the increased number of shares available under the 2014 Plan and the 2014 ESPP each 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. 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, or the IRC, 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 $7.2 million and a permanent decrease in federal research tax credit carryforwards in the amount of $0.2 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 resolution adopted by the board 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. Further, no stockholder is permitted to cumulate votes at any election of directors because this right is not included in our amended and restated certificate of incorporation.

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.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is the sole and exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is the sole and exclusive forum for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of fiduciary duty owed by any of our directors, officers, or other employees to us or to our stockholders, (3) any action asserting a claim against us arising under the Delaware General Corporation Law or under our amended and restated certificate of incorporation or bylaws, or (4) any action against us asserting a claim governed by the internal affairs doctrine. The choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers, or other employees, which may discourage such lawsuits against us and our directors, officers, and other employees. Alternatively, if a court were to find the choice of forum provision contained in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could harm our business, operating results and financial condition.

Item 2. ***Unregistered Sales of Equity Securities and Use of Proceeds***

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	8-K	2/5/2014	3.1	
3.2	Amended and Restated Bylaws	8-K	2/5/2014	3.2	
10.1§	Amendment No. 8 to Collaboration and License Agreement, effective as of July 4, 2019, between Ultragenyx Pharmaceutical Inc. and Kyowa Kirin Co., Ltd. (formerly, Kyowa Hakko Kirin Co., Ltd.)				X
10.2§	Amended and Restated Collaboration and License Agreement, dated June 3, 2019, between Ultragenyx Pharmaceutical Inc. and Bayer Healthcare LLC				X
10.3	Addendum #6 to Standard Lease, effective as of April 29, 2019, by and between Ultragenyx Pharmaceutical Inc. and Condiotti Enterprises, Inc.				X
10.4#	Offer Letter, dated May 16, 2017, by and between Ultragenyx Pharmaceutical Inc. and Erik Harris.				X
10.5#	Addendum #1, dated August 8, 2017, to Offer Letter dated May 16, 2017 between Ultragenyx Pharmaceutical Inc. and Erik Harris.				X
10.6#	Addendum #2, dated June 19, 2019, to Offer Letter dated May 16, 2017 between Ultragenyx Pharmaceutical Inc. and Erik Harris.				X
31.1	Certification of Principal Executive Officer Required Under Rule 13a-14(a) or Rule 15d-14(a) of the Exchange Act				X
31.2	Certification of Principal Financial Officer Required Under Rule 13a-14(a) or Rule 15d-14(a) of the Exchange Act				X
32.1*	Certification of Principal Executive Officer and Principal Financial Officer Required Under Rule 13a-14(b) or Rule 15d-14(b) of the Exchange Act and 18 U.S.C. 1350				X
101.INS	XBRL Instance Document, formatted in Inline XBRL				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
104	The cover page from the Company's Quarterly Report on Form 10-Q for the quarter ended June 30, 2019, formatted in Inline XBRL.				

§ Certain confidential portions of this exhibit were omitted by means of marking such portions with asterisks because the identified confidential portions (i) are not material and (ii) would be competitively harmful if publicly disclosed.

# Indicates management contract or compensatory plan.

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

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 1, 2019

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

Date: August 1, 2019

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

Date: August 1, 2019

By: /s/ Theodore A. Huizenga
Theodore A. Huizenga
Vice President and Corporate Controller
(Principal Accounting Officer)

Exhibit 10.1

[***] = CERTAIN CONFIDENTIAL INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY BRACKETS, HAS BEEN OMITTED BECAUSE THE INFORMATION (I) IS NOT MATERIAL AND (II) WOULD BE COMPETITIVELY HARMFUL IF PUBLICLY DISCLOSED.

AMENDMENT NO. 8 TO COLLABORATION AND LICENSE AGREEMENT

This Amendment No. 8 to the Collaboration and License Agreement ("**Amendment**") is made and entered into by and between Kyowa Kirin Co., Ltd. (formerly, Kyowa Hakko Kirin Co., Ltd.), a company organized and existing under the laws of Japan, with an address at 1-9-2 Otemachi, Chiyoda-ku, Tokyo, 100-0004, Japan ("**KHK**") and Ultragenyx Pharmaceutical Inc., a company organized and existing under the laws of the State of Delaware, with an address at 60 Leveroni Court, Novato, California 94949, USA ("**UGNX**").

RECITALS

A. WHEREAS, KHK and UGNX entered into a Collaboration and License Agreement effective as of August 29, 2013, an Amendment No. 1 to Collaboration and License Agreement effective as of August 24, 2015, an Amendment No. 2 to Collaboration and License Agreement effective as of November 28, 2016, an Amendment No. 3 to Collaboration and License Agreement effective as of September 29, 2017, an Amendment No. 4 to Collaboration and License Agreement effective as of January 29, 2018, an Amendment No. 5 to Collaboration and License Agreement effective as of April 30, 2018, an Amendment No. 6 to Collaboration and License Agreement effective as of February 1, 2019 and an Amendment No. 7 to Collaboration and License Agreement effective as of December 5, 2018 (collectively, the "**Collaboration Agreement**").

B. WHEREAS, both Parties wish to further amend the Collaboration Agreement as set forth below.

C. NOW, THEREFORE, in consideration of the mutual covenants and premises herein contained, the Parties agree as follows:

1. This Amendment shall be effective as of July 4, 2019 (the "**Amendment Effective Date**").

2. Any capitalized terms that are not defined in this Amendment will have their respective meanings set forth in the Collaboration Agreement.

3. A new Sections 4.9.3.1, 4.9.3.2 and 4.9.3.3 shall be added that provides as follows:

" 4.9.3.1 **Pre-filled Syringe.** In accordance with Section 4.9.3, the Parties agree that pre-filled syringe Licensed Products (the "**Pre-filled Syringe**") will be Developed for obtaining Marketing Approval in the U.S. and the European Core Territory. KHK shall be responsible for performing (i) CMC activities including manufacturing, stability, tech transfer and lab study, and (ii) clinical and regulatory activities necessary to obtain the regulatory approval for the Pre-filled Syringe in the European Core Territory, in accordance with the attached Exhibit A. [***] shall bear the costs in connection with such activities including [***]. Up and until the Profit Share Transition Date, UGNX shall be responsible for performing certain

clinical and regulatory activities necessary to obtain the Marketing Approval for the Pre-filled Syringe in the U.S., including the Human Factor Engineering (HFE) study, in accordance with the attached Exhibit A (the "**UGNX Activities**"). For the avoidance of doubt, the Parties acknowledge and agree that the UGNX Activities as of the Amendment Effective Date do not include any clinical bridging study. In the case a clinical bridging study is required in the US, the Parties shall discuss in good faith with regards to the responsibilities and cost allocations for such study. UGNX shall bear the same responsibilities and obligations to the UGNX Activities as UGNX bears in Articles 4 and 5 of the Collaboration Agreement. UGNX and KHK shall [***] the costs in connection with the UGNX Activities including [***]. The timeline of the Pre-filled Syringe Development in the U.S. (the "**Timeline**") is attached hereto as Exhibit B. In the event any of the UGNX Activities need to continue beyond the Profit Share Transition Date, the Parties shall separately discuss and agree upon development and cost-sharing of such continued activities.

4.9.3.2 **Revised Plan.** In case of a major change in budget of the UGNX Activities (exceeding [***] of the approved budget), or a major change in the Timeline ([***]), the JSC shall review and approve the revised budget, Timeline or Pre-filled Syringe Development plan in the U.S. The JSC's decision will be made in accordance with Section 3.5, provided that [***] will have the authority to make the final decision with regards to [***], other than the [***].

4.9.3.3 **Development in Canada.** In case both Parties agree to Develop Pre-filled Syringe in Canada, the Parties may seek Marketing Approval of Pre-filled Syringe in Canada. In such case the responsibilities and cost allocations of the Parties for Canada will follow that of the U.S. as described in Sections 4.9.3.1 and 4.9.3.2.

4. Except as expressly provided in this Amendment, all other terms, conditions and provisions of the Collaboration Agreement shall continue in full force and effect as provided therein.

IN WITNESS WHEREOF, the Parties have executed this Amendment No. 8 to Collaboration and License Agreement to be effective as of the Amendment Effective Date.

KYOWA KIRIN CO., LTD.

By: /s/ Yasuo Fujii
Name: Yasuo Fujii
Title: Director, Business Development Dept.

ULTRAGENYX PHARMACEUTICAL INC.

By: /s/ Thomas Kassberg
Name: Thomas Kassberg
Title: Chief Business Officer

Exhibit A

[***]

Exhibit B

[***]

Exhibit 10.2

[***] = CERTAIN CONFIDENTIAL INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY BRACKETS, HAS BEEN OMITTED BECAUSE THE INFORMATION (I) IS NOT MATERIAL AND (II) WOULD BE COMPETITIVELY HARMFUL IF PUBLICLY DISCLOSED.

Execution Copy

AMENDED AND RESTATED COLLABORATION AND LICENSE AGREEMENT

This AMENDED AND RESTATED COLLABORATION AND LICENSE AGREEMENT ("Agreement") is entered into as of June 3, 2019 ("A&R Effective Date") by and between Ultragenyx Pharmaceutical Inc., a corporation organized under the laws of the State of Delaware, with offices at 60 Leveroni Court, Novato, CA 94949 ("Dimension"), and Bayer HealthCare LLC, a limited liability company organized under the laws of the State of Delaware, with offices at 455 Mission Bay Blvd South, San Francisco, CA 94158 ("Bayer"). Dimension and Bayer are hereinafter referred to individually as a "Party" and collectively as the "Parties."

WHEREAS, Dimension Therapeutics, Inc. was granted exclusive rights by its licensor, ReGenX Biosciences, LLC ("ReGenX") under certain patents and know-how which have been licensed to ReGenX from its upstream licensors, Glaxo SmithKline (as successor in interest to SmithKline Beecham Corporation, "GSK") and the Trustees of the University of Pennsylvania ("UPenn"), pertaining to various recombinant adeno-associated virus vectors and their use in gene therapy treatments for hemophilia;

WHEREAS, as of March 31, 2019, Dimension Therapeutics, Inc. has been merged with and into Ultragenyx Pharmaceutical Inc., and Dimension Therapeutics, Inc. has ceased its separate corporate existence;

WHEREAS, as a result of such merger, references made to "Dimension" herein shall be treated as references to Ultragenyx Pharmaceutical Inc.;

WHEREAS, Dimension has expertise in the research, identification and early stage development of gene therapy treatments in humans;

WHEREAS, Bayer is a leading pharmaceutical company that has technology and expertise in developing and commercializing therapies for human genetic diseases, including hemophilia;

WHEREAS, the Parties are party to that certain Collaboration and License Agreement, dated as of June 18, 2014 (such agreement, the "Original Agreement", and the date thereof, the "Original Effective Date"), under which the Parties entered into a collaboration for the purpose of researching, developing and commercializing adeno-associated virus based gene therapy products for treatment of hemophilia A; and

WHEREAS, the Parties desire to amend and restate the Original Agreement in its entirety and replace the Original Agreement with this Agreement.

NOW, THEREFORE, in consideration of the promises and covenants contained in this Agreement, and intending to be legally bound, the Parties hereby agree as follows:

ARTICLE 1: DEFINITIONS

1.1 "[***] Expense Report" has the meaning set forth in Section 2.5.1.

1.2 "Affiliate" means any legal entity directly or indirectly controlling, controlled by, or under common control with another entity. For purposes of this Agreement, an entity shall be deemed to "control" another entity if it owns or controls, directly or indirectly, more than 50% of the outstanding voting securities of such other entity, or has the right to receive more than 50% of the profits or earnings of such other entity, or has the right to control the policy decisions of such other entity.

1.3 "Antihemophilic Factor" means the MAA-approved exogenous recombinant antihemophilic factor (i.e., rFVIII) labeled for use in the Field and administered by or on behalf of Bayer, its Affiliates or Sublicensees to a patient for prophylactic and non-interventional purposes.

1.4 "Biosimilar Treatment" means on a country-by-country basis, a treatment that is introduced in the applicable country in the Territory by an entity other than Bayer or a Sublicensee or their respective Affiliates, which (a) contains or incorporates a therapeutic or prophylactic agent that is the same or equivalent (by FDA, EMA or other applicable Regulatory Authority standards, on a country-by-country basis) to the Licensed GT Product; and (b) has been granted Regulatory Approval by an abridged procedure in reliance in whole or in part on (i) the prior Regulatory Approval in such country of the Licensed GT Product and Licensed Treatment, or (ii) the safety and efficacy data generated for the prior Regulatory Approval for such Licensed Treatment or Licensed GT Product.

1.5 "Business Day" means a day other than a Saturday, Sunday or any day on which commercial banks located in California, New Jersey, and Massachusetts are authorized or obligated by law to be closed.

1.6 "Calendar Quarter" means each three-month period or any portion thereof, beginning on January 1, April 1, July 1, and October 1.

1.7 "Change of Control" means, with respect to a Party (the "Acquired Entity"):

(a) any sale, exchange, transfer, or issuance to or acquisition in one transaction or a series of related transactions by one or more Third Parties of shares representing more than fifty percent (50%) of the aggregate ordinary voting power entitled to vote for the election of directors represented by the issued and outstanding stock of the Acquired Entity or any Affiliate that directly or indirectly controls the Acquired Entity, whether such sale, exchange, transfer, issuance or acquisition is made directly or indirectly, by merger or otherwise, or beneficially or of record;

(b) a merger, consolidation, reorganization, business organization, joint venture or similar transaction under applicable Law of the Acquired Entity with a Third Party in which the shareholders of the Acquired Entity or any Affiliate that directly or indirectly controls the Acquired Entity immediately prior to such transaction do not continue to hold immediately following the closing of such transaction at least fifty

percent (50%) of the aggregate ordinary voting power entitled to vote for the election of directors represented by the issued and outstanding stock of the entity surviving or resulting from such transaction; or

(c) a sale or other disposition of all or substantially all of the assets of the Acquired Entity to one or more Third Parties in one transaction or a series of related transactions.

For purposes of clarity, the term "Change of Control," with respect to a Party, is not intended to include: (i) an underwritten public offering of Dimension's common stock pursuant to a Registration Statement on Form S-1 under the 1933 Act, as amended; or (ii) any sale of shares of capital stock of a Party, in a single transaction or series of related transactions, principally for bona fide equity financing purposes in which such Party issues new securities solely to institutional investors for cash or the cancellation or conversion of indebtedness of such Party or a combination thereof for the purpose of financing the operations and business of such Party.

1.8 "Commercialization" or "Commercialize" means any and all activities directed to the marketing, promotion, offering for sale and sale of a pharmaceutical or therapeutic product, both, to the extent permitted by law, before Regulatory Approval has been obtained, and after, and all commercial manufacturing activities, as well as any post-Regulatory Approval clinical trials. When used as a verb, "to Commercialize" and "Commercializing" means to engage in Commercialization and "Commercialized" has a corresponding meaning.

1.9 "Commercially Reasonable Efforts" means: (a) with respect to Dimension's obligation under this Agreement to research and develop GT Products in the Field, the level of efforts normally used by a similarly situated biopharmaceutical company in meeting the objective(s) set forth in the Research Plan; and (b) with respect to Bayer's obligation under this Agreement to develop a GT Product and Commercialize a Licensed GT Product and Licensed Treatments, the level of efforts and resources normally used by Bayer for a similar product owned or controlled by it of similar market potential at a similar stage in the development or life of such product, taking into account issues of safety, efficacy, product profile, the competitiveness of the marketplace, the proprietary position of the product, the regulatory structure involved, profitability of the product and other relevant medical, ethical and commercial factors.

1.10 "Compound/Vector" means any gene transfer agent that contains a gene that expresses either (a) the Factor VIII protein, or (b) any variant of the Factor VIII protein (*e.g.*, [***]).

1.11 "Confidential Information" means and includes all technical information, inventions, developments, discoveries, software, Know-How, methods, techniques, formulae, animate and inanimate materials, data, processes, finances, business operations or affairs, and other proprietary ideas, whether or not patentable or copyrightable, of either Party that are (a) marked or otherwise identified by the Disclosing Party as confidential or proprietary at the time of disclosure in writing; or (b) if disclosed orally, visually, or in another non-written form, identified by the Disclosing Party as confidential at the time of disclosure; or (c) if not marked as

provided in clause (a) or otherwise identified as provided in clause (b), would reasonably be understood by a Third Party receiving such information as being confidential or proprietary in nature. The Parties acknowledge that (i) the terms and conditions of this Agreement and (ii) the records and reports referred to in Section 6.5 will be deemed the Confidential Information of both Parties, regardless of whether such information is marked or identified as confidential. In addition, information provided to Bayer pursuant to the provisions of Section 10.2 will be deemed the Confidential Information of Dimension, regardless of whether such information is marked or identified as confidential. Notwithstanding the foregoing, Confidential Information will not include the following, in each case, to the extent evidenced by competent written proof of the Receiving Party:

1.11.1 information that was already known to the Receiving Party other than under an obligation of confidentiality at the time of disclosure by the Disclosing Party;

1.11.2 information that was generally available to the public or otherwise part of the public domain at the time of its disclosure to the Receiving Party;

1.11.3 information that became generally available to the public or otherwise part of the public domain after its disclosure, other than through any act or omission of the Receiving Party in breach of this Agreement;

1.11.4 information that is independently discovered or developed by the Receiving Party without the use of Confidential Information of the Disclosing Party; or

1.11.5 information that was disclosed to the Receiving Party, other than under an obligation of confidentiality, by a Third Party who had no obligation to the Disclosing Party not to disclose such information to others.

1.12 "Control" or "Controlled" means with respect to any Know-How, Patent Rights or other intellectual property right, that a Party has a license (other than a license granted to such Party under this Agreement) to such Know-How, Patent Rights or other intellectual property right and, in each case, has the ability to grant to the other Party access, a license, or a sublicense (as applicable) to the foregoing on the terms and conditions set forth in this Agreement without violating the terms of any agreement or other legally enforceable arrangement with any Third Party.

1.13 "Controlled Affiliate" means, as to any Party, an Affiliate under the direct or indirect control of such Party, within the meaning of Section 1.2.

1.14 "Controlling Affiliate" means, as to any Party, an Affiliate that directly or indirectly controls such Party within the meaning of Section 1.2.

1.15 "Cost Overrun" has the meaning set forth in Section 2.5.3.

1.16 "Demonstration of Clinical POC" means that the criteria set forth in Exhibit E have been met, as determined by the Parties in accordance with Section 2.11.4.

1.17 "Dimension Know-How" means any Know-How that (a) is Controlled by Dimension or any of its Controlled Affiliates as of the Original Effective Date or comes into the Control of Dimension or any of its Controlled Affiliates after the Original Effective Date and at any time during the term of this Agreement (other than through the grant of a license by Bayer hereunder), (b) is reasonably necessary or useful for the development, manufacture or Commercialization of Licensed GT Products, Licensed Treatments, or for Bayer to perform its obligations under this Agreement, and (c) is neither (i) Sublicensed Know-How, nor (ii) any Manufacturing Technology which is other than [***] Know-How, and that comes into the Control of Dimension under the ReGenX Agreement or another agreement with ReGenX. "Dimension Know-How" includes but is not limited to all biological, chemical, structure-activity relationship, pharmacological, toxicological, manufacturing, preclinical and clinical information relating to Licensed GT Products or the Compound/Vector used in such product. For the avoidance of doubt, Dimension Know-How includes Dimension's interest in the Joint Inventions, but does not include any Patent Rights. It is expressly understood that, in the event of a Change of Control of Dimension, the Dimension Know-How shall not include any Know-How that is owned or controlled by a Controlling Affiliate and (i) existing prior to the closing of such Change of Control, or (ii) developed by or on behalf of such Controlling Affiliate after such Change of Control without the use of the Dimension Know-How in existence prior to the closing of such Change of Control, or (iii) developed by or on behalf of such Controlling Affiliate after such Change of Control and not directly related to any Licensed GT Product or any Compound/Vector used therein. It is understood that the burden shall be on Dimension to establish that the foregoing exclusions apply, and such exclusions shall apply only if the Controlling Affiliate remains a separate legal entity to Dimension.

1.18 "Dimension Manufacturing Patents" means all Patent Rights that (a) are not Sublicensed Patents, (b) come into the ownership or Control of Dimension or its Controlled Affiliates after the Original Effective Date and during the term of this Agreement (other than through the grant of a license by Bayer hereunder), and (c) claim inventions relating to the process of manufacture of any Licensed GT Product, Licensed Treatment or any Compound/Vector, which inventions were not generated in the conduct of the manufacturing development set forth in the Research Plan, but were generated by or on behalf of Dimension prior to Bayer's submission of the first MAA for a Licensed GT Product. It is expressly understood that in the event of a Change of Control of Dimension, the Dimension Manufacturing Patents shall not include any Patent Rights owned or controlled by a Controlling Affiliate and (i) existing prior to the closing of such Change of Control of Dimension, (ii) existing after the closing of such Change of Control and claiming inventions made by or on behalf of such Controlling Affiliate prior to the closing of such Change of Control, (iii) claiming only inventions made after such Change of Control without the use of the Dimension Know-How in existence prior to the closing of such Change of Control, or (iv) claiming only inventions made after such Change of Control and not directly related to the Licensed Treatment, Licensed GT Product or the Compound/Vector used therein. It is understood that the burden shall be on Dimension to establish that the foregoing exclusions apply, and such exclusions shall apply only if the Controlling Affiliate remains a separate legal entity to Dimension.

1.19 "Dimension Patents" means all Patent Rights that (a) are not Sublicensed Patents, (b) are not Dimension Manufacturing Patents, (c) are owned or Controlled by Dimension or its Controlled Affiliates as of the Original Effective Date or that come into the ownership or Control

of Dimension or its Controlled Affiliates after the Original Effective Date and during the term of this Agreement (other than through the grant of a license by Bayer hereunder), and (d) cover (i) the development, use or Commercialization of any Licensed GT Product, Licensed Treatment or any Compound/Vector used therein or (ii) the manufacture of any Licensed GT Product, Licensed Treatment or any Compound/Vector used therein to the extent such Patent Rights cover inventions that were generated in the conduct of the manufacturing development as set forth in the Research Plan. For the avoidance of doubt, Dimension Patents include Dimension's interest in the Joint Patents. Dimension Patents as of the Original Effective Date are listed in Exhibit A. It is expressly understood that in the event of a Change of Control of Dimension, the Dimension Patents shall not include any Patent Rights owned or controlled by a Controlling Affiliate and (i) existing prior to the closing of such Change of Control of Dimension, (ii) existing after the closing of such Change of Control and claiming inventions made by or on behalf of such Controlling Affiliate prior to the closing of such Change of Control, (iii) claiming only inventions made after such Change of Control without the use of the Dimension Know-How in existence prior to the closing of such Change of Control, or (iv) claiming only inventions made after such Change of Control and not directly related to the Licensed Treatment, Licensed GT Product or the Compound/Vector used therein. It is understood that the burden shall be on Dimension to establish that the foregoing exclusions apply, and such exclusions shall apply only if the Controlling Affiliate remains a separate legal entity to Dimension.

1.20 "Disclosing Party" has the meaning set forth in Section 8.1.

1.21 Intentionally Omitted.

1.22 "Existing Licenses" means the GSK Agreement and Penn Agreement.

1.23 "FDA" means the United States Food and Drug Administration, or a successor agency in the United States with responsibilities comparable to those of the United States Food and Drug Administration.

1.24 "Field" means any and all human therapeutic uses to treat and diagnose hemophilia A (and expressly not hemophilia B or any other form of hemophilia other than hemophilia A).

1.25 "First Commercial Sale" means, on a country-by-country basis (a) the first commercial sale of a Licensed Treatment by Bayer, its Sublicensees or their respective Affiliates to a person or entity who is not Bayer, its Sublicensees or their respective Affiliates in such country after grant of Regulatory Approval in the applicable country or jurisdiction, provided that where such a first commercial sale has occurred in a country for which pricing approval is necessary for widespread sale, then such sale shall not be deemed a First Commercial Sale until such pricing approval has been obtained; or (b) any compassionate use or named patient basis sale in such country, following the date upon which cumulative Net Sales (across all countries in the Territory) received from any compassionate use or named patient program by Bayer, its Affiliate or Sublicensees equals [***] Dollars ($[***]), provided the Licensed Treatment Administration Sales and Licensed Treatment Monitoring Sales with respect to the Licensed GT Products administered pursuant to such programs is greater than the fully loaded costs of such Licensed GT Products. For the avoidance of doubt, supply of Licensed GT Product as samples

or to patients for clinical trials or other similar purposes shall not be considered a First Commercial Sale.

1.26 "GSK Agreement" means that certain License Agreement entered into between ReGenX and GSK, effective on March 6, 2009, as amended by that certain Amendment to License Agreement dated April 15, 2009, and as amended from time to time.

1.27 "GT Product" means:

(a) a pharmaceutical product or medical therapy for repairing, modulating the expression of, or inserting a functional version of, the Factor VIII protein but not any other target or locus, which product or therapy (1) contains or employs at least one Compound/Vector and (2) does not contain or employ any other gene or variant of such gene that is other than the Factor VIII protein or a variant of the Factor VIII protein; or

(b) a pharmaceutical product or medical therapy that contains or employs a human cell or tissue made using a product or therapy described in (a).

1.28 "IND" means (a) an Investigational New Drug Application as defined in the U.S. Federal Food, Drug, and Cosmetic Act, as amended, and regulations promulgated thereunder or any successor application or procedure required to initiate clinical testing of a GT Product in humans in the United States; (b) a counterpart of an Investigational New Drug Application that is required in any other country or regulatory jurisdiction other than the United States before beginning clinical testing of the GT Product in humans in such country or regulatory jurisdiction; and (c) all supplements and amendments to any of the foregoing.

1.29 "Joint Inventions" has the meaning set forth in Section 10.1.

1.30 "Joint Patents" has the meaning set forth in Section 10.1.

1.31 "Joint Project Team" or "JPT" has the meaning set forth in Section 4.3.

1.32 "Joint Research and Development Committee" or "JRDC" means the research and development oversight committee comprised of representatives of Dimension and Bayer, as further described in Section 4.2.

1.33 "Joint Steering Committee" or "JSC" means the oversight committee comprised of two (2) representatives each of Dimension and Bayer, as further described in Section 4.1.

1.34 "Know-How" means any and all ideas, information, know-how, data, research results, writings, inventions, discoveries, and other technology (including any proprietary materials), whether or not patentable or copyrightable.

1.35 "Laws" means all laws, statutes, rules, regulations, ordinances and other pronouncements having the effect of law of any federal, national, multinational, state, provincial, county, city or other political subdivision, domestic or foreign.

1.36 "Licensed Back Improvements" means any patentable modifications or improvements developed by Bayer, any of its Affiliates, or any Sublicensees to any vector that is the subject of a claim within the Licensed Patents.

1.37 "Licensed GT Product" has the meaning set forth in Section 2.11.

1.38 "Licensed Know-How" means the Dimension Know-How and the Sublicensed Know-How.

1.39 "Licensed Patents" means the Dimension Patents and the Sublicensed Patents.

1.40 "Licensed Technology" means, collectively, the Licensed Patents and the Licensed Know-How.

1.41 "Licensed Treatment" means any (a) Licensed GT Product in any and all modes of administration, presentations, formulations and dosages, that either (i) the manufacture, use, sale, offer for sale, or import of which is covered by, or which, in the absence of the licenses granted pursuant to this Agreement, would infringe, at least one Valid Claim of a Sublicensed Patent or Dimension Patent, in the country of manufacture, use, sale, offer for sale, or import; or (ii) is generated through the use of Sublicensed Know-How or Dimension Know-How; and/or (b) service with respect to the administration to patients of any Licensed GT Product described in clause (a)(i) or (a)(ii) above in this Section 1.41; and/or (c) service with respect to the monitoring as to the effectiveness or safety in patients of any Licensed GT Product described in clause (a)(i) or (a)(ii) above in this Section 1.41.

1.42 "Licensed Treatment Administration Sales" means, with respect to a given patient in the Field to whom a Licensed Treatment is administered, the gross amount invoiced by Bayer, its Affiliate or Sublicensee to Third Parties, and recognized in their respective accounting books as income, for the initial administration of such Licensed Treatment to such patient.

1.43 "Licensed Treatment Monitoring Sales" means, with respect to a given patient in the Field to whom a Licensed Treatment has been administered, the gross amounts invoiced to Third Parties by Bayer, its Affiliates or Sublicensees on or after receipt of the Licensed Treatment Administration Sale, and recognized in their respective accounting books as income, for either services rendered in the monitoring of such patient, and/or the continuing effectiveness of the Licensed GT Product with respect to such patient.

1.44 "Licensed Treatment Sales" means with respect to a given period, all Licensed Treatment Administration Sales and all Licensed Treatment Monitoring Sales during such period, minus all Post-Administration Antihemophilic Factor administered during such period. For illustrative purposes only, Exhibit B sets forth examples for calculating Licensed Treatment Sales based on Licensed Treatment Administration Sales, Licensed Treatment Monitoring Sales, and any Post-Administration Antihemophilic Factor administered.

1.45 "MAA" means either a New Drug Application filed with the FDA as described in 21 C.F.R. § 314, a Biological License Application (BLA) pursuant to 21 C.F.R. § 601.2, or any equivalent or any corresponding application in any country or regulatory jurisdiction other than the United States.

1.46 "Major Market Country" means the [***].

1.47 "Manufacturing Technology" means any and all Patent Rights, Know-How, and all intellectual property rights associated therewith, and including all tangible embodiments thereof, that are necessary or useful for the manufacture of any Licensed GT Product or Compound/Vector used therein, or research or commercial reagents related thereto, including manufacturing processes, technical information relating to the methods of manufacture, protocols, standard operating procedures, batch records, assays, formulations, quality control data, specifications, scale up, any and all improvements, modifications, and changes thereto, and any and all activities associated with such manufacture. Any and all chemistry, manufacturing, and controls (CMC), drug master files (DMFs), or similar materials provided to regulatory authorities and the information contained therein are deemed Manufacturing Technology.

1.48 "Net Sales" means, with respect to a given period, the Licensed Treatment Sales made during such period less the following deductions that are directly attributable to Licensed Treatment Administration Sales or, to the extent applicable, any Licensed Treatment Monitoring Sales:

1.48.1 [***];

1.48.2 [***] imposed upon the sale of a Licensed GT Product and [***];

1.48.3 [***] in connection with the Licensed Treatment Administration Sales;

1.48.4 [***] of a Licensed GT Product; and

1.48.5 [***] in connection with Licensed Treatment Administration Sales.

Sales between and among Bayer and its Affiliates or Sublicensees of Licensed GT Products shall be excluded from the computation of Net Sales, except where [***], but Net Sales shall include [***].

For the purpose of calculating Net Sales, the Parties recognize that: (a) [***]; and (b) in such cases, [***].

In the event the Licensed GT Product is sold [***], Net Sales for such [***]. If, on a country-by-country basis, [***], then Net Sales will be [***]. If, on a country-by-country basis, [***].

[***] shall not be considered in determining Net Sales; provided, however, that [***].

All amounts used to calculate Licensed Treatment Sales shall be applied in accordance with IFRS, [***].

1.49 "Operating Plan" has the meaning assigned to it in Section 2.3.1.

1.50 "Patent Rights" means issued patents and pending patent applications in any country or region, including all provisional, non-provisionals, substitutions, continuations,

continuations-in-part, divisionals, renewals and all patents granted thereon, and all reissues, reexaminations, extensions, confirmations, revalidations, registrations and patents of addition thereof, including supplementary protection certificates.

1.51 "Penn Agreement" means that certain License Agreement entered into between ReGenX and UPenn, effective on February 24, 2009, as amended by that letter agreement dated March 6, 2009, and as amended from time to time.

1.52 "Phase II/III Trial" means a human clinical trial of a Licensed GT Product according to 21 C.F.R. 312.21(b) and (c) (or their successor regulations or any equivalent regulation with respect to jurisdictions outside of the United States).

1.53 "Pivotal Clinical Trial" means a human clinical trial of a Licensed GT Product and/or Licensed Treatment (a) [***]; or (b) the Phase III portion (as defined in the protocol) of a Phase II/III Trial or other similar designation as approved by the FDA, or the corresponding regulations outside the U.S.

1.54 "POC Data" means the data from the POC Trial necessary to assess Demonstration of Clinical POC (whether or not there is a subsequent positive determination of Demonstration of POC).

1.55 "Post-Administration Antihemophilic Factor" means, [***].

1.56 "Proof of Concept Trial" or "POC Trial" means the Phase I human proof of concept trial in patients for a GT Product as described in the First IND (as defined in Section 2.13). For clarity, the protocol for the POC Trial may be amended provided that the part of the POC Trial in which the POC Data are generated shall not be amended in such a way that it adversely impacts the timing or generation of the POC Data.

1.57 "Prosecute" means preparation, filing, and prosecuting patent applications and maintaining patents, including any reexaminations, reissues, inter partes reviews, post-grant reviews, oppositions, and interferences.

1.58 "Receiving Party" has the meaning set forth in Section 8.1.

1.59 "ReGenX Agreement" means that certain License Agreement entered into between Dimension and ReGenX, effective on October 31, 2013, as amended from time to time.

1.60 "ReGenX Improvements" means any patent or patent application that meets all of the following criteria:

(a) is directed to any of: the composition of recombinant adeno-associated virus vectors, methods of use of such vectors, or methods of developing such vectors, but, in each case, only to the extent of such claims; and

(b) is reasonably necessary for any of: the use, sale, offer for sale, or import of Licensed Products in the Field (as such capitalized terms are defined in the ReGenX Agreement);

provided that "ReGenX Improvements" will not include any Manufacturing Technology.

1.61 "Regulatory Approval" means, with respect to particular country or territory, the approval of the MAA or similar approval required to sell a Licensed GT Product and/or Licensed Treatment in such country or territory, including, where required by applicable Law, pricing and reimbursement approval.

1.62 "Regulatory Authority" means any country, federal, supranational, state or local regulatory agency, department, bureau or other governmental or regulatory authority having the administrative authority to regulate the development or marketing of pharmaceutical products in any country or other jurisdiction, and includes the FDA in the US and the European Medicines Agency in the EU.

1.63 "Research Budget" means the budget attached to this Agreement as Exhibit D-3, as may be amended from time to time as provided for in this Agreement, and covering [***]. The Research Budget as of the A&R Effective Date is set forth in Exhibit D-3.

1.64 "Research Plan" means the research plan addressing the activities to be performed hereunder, and as such research plan may be amended in writing from time to time. The Research Plan shall contain (a) a description of the process for identifying the criteria for selecting GT Products as potential clinical candidates, [***], (b) a description of the specific activities to be performed by the Parties, including the pre-clinical and regulatory work necessary to commence the POC Trial and clinical work necessary for receipt of the POC Data, (c) the primary and secondary endpoints of the POC Trial, (d) manufacturing / CMC development for purposes of providing the POC Trial Material (as defined below), (e) projected timelines for completion of the described activities, and (f) the Research Budget. The Research Plan as of the A&R Effective Date is set forth in Exhibit D-1.

1.65 "Research Program" means the research collaboration between the Parties, under the direction and oversight of the JRDC, aimed at the discovery of one or more suitable Licensed GT Products for hemophilia A and moving one such Licensed GT Product forward into the POC Trial and receipt of the POC Data, pursuant to the Research Plan during the Research Term.

1.66 "Research Term" means the period following the Original Effective Date for the Parties to conduct and complete the Research Plan, unless earlier terminated as provided under Section 2.2 of this Agreement.

1.67 "Retained Rights" has the meaning set forth in Section 5.3.

1.68 "Royalty Term" has the meaning set forth in Section 6.4.2.

1.69 "Sublicensed Know-How" means any Know-How that (a) is Controlled by Dimension as of the Original Effective Date or that comes into the Control of Dimension after the Original Effective Date and during the term of this Agreement, (b) is licensed to Dimension under the ReGenX Agreement, and (c) is reasonably necessary for the use, sale, offer for sale, or import of POC Trial Material or Licensed GT Products in the Field; provided that "Sublicensed Know-How" will not include any Manufacturing Technology, other than [***] Know-How, that comes into the Control of Dimension under the ReGenX Agreement and which otherwise meets

the foregoing criteria; and provided further that "Sublicensed Know-How" does not include any Patent Rights.

1.70 "Sublicensed Patents" means (a) the Patent Rights listed in Exhibit A, and (b) all other Patent Rights that cover or claim any POC Trial Material, Licensed GT Product or Licensed Treatment or component thereof, or use thereof in the Field, and that (i) are Controlled by Dimension as of the Original Effective Date or that come into the Control of Dimension after the Original Effective Date and during the term of this Agreement, and (ii) are licensed to Dimension under the ReGenX Agreement, provided that "Sublicensed Patents" will not include any claim of a patent or patent application owned or controlled by ReGenX covering any Manufacturing Technology.

1.71 "Sublicensed Technology" means, collectively, the Sublicensed Patents and Sublicensed Know-How.

1.72 "Sublicensee" means any Third Party or Affiliate to whom Bayer grants a sublicense of some or all of the rights granted to Bayer under this Agreement as permitted by this Agreement.

1.73 "Territory" means the entire world.

1.74 "Third Party" means any person or entity other than a Party to this Agreement or Affiliates of a Party to this Agreement.

1.75 "[***] Know-How" means unpatented Know-How that, as of October 30, 2013, (a) is Controlled by ReGenX pursuant to the Existing Licenses or pursuant to ReGenX's ownership thereof, and (b) is directed [***]; provided that, notwithstanding the scope of the license grant in Section 5.1(a), any rights granted to Bayer under this Agreement with respect to the [***] Know-How will be limited to use of such Know-How in the Field.

1.76 "Valid Claim" means a claim of an issued and unexpired patent (including any patent claim the term of which is extended by any extension, supplementary protection certificate, patent term restoration, or the like) included within the Sublicensed Patents or Dimension Patents or a claim of a pending patent application included within the Sublicensed Patents or Dimension Patents, which has not lapsed, been abandoned, been held revoked, or been deemed unenforceable or invalid by a non-appealable decision or an appealable decision from which no appeal was taken within the time allowed for such appeal of a court or other governmental agency of competent jurisdiction and, in the case of a pending application, that has been pending for less than [***] years from the priority date of the claim.

ARTICLE 2: RESEARCH AND DEVELOPMENT PROGRAM

2.1 Collaboration Overview. Dimension and Bayer shall collaborate during the Research Term for the purpose of researching and developing, until Demonstration of Clinical POC, of at least one GT Product for use in the Field, which Bayer shall have the exclusive right to further develop, seek Regulatory Approval for, and if successful, Commercialize in the Territory, all in accordance with this Agreement. To that end, under the oversight of the JSC and JRDC, Dimension will be responsible for performing those research and development activities

allocated to it in the Research Plan, and subject to any limitations set forth in Section 2.5, Bayer shall fund Dimension's efforts under the Research Plan in accordance with the Research Budget and shall conduct the POC Trial, including distributing in finished form the POC Trial Material for the conduct thereof. Except as otherwise agreed by the Parties pursuant to Section 3.4, following completion of the transition plan set forth in Exhibit G (the "Transition Plan"), Bayer will be solely (except as expressly stated in this Agreement, including in Section 3.4) responsible, at its own cost, for performing any remaining activities set forth in the Research Plan and all subsequent development and Commercialization activities for each Licensed GT Product in the Field and in the Territory.

2.2 Responsibilities of the Parties during the Research Term.

2.2.1 During the Research Term and subject to the oversight of the JRDC, Dimension shall be responsible only for carrying out, by itself or through a Third Party, the tasks assigned to Dimension in the Research Plan. Dimension shall use Commercially Reasonable Efforts in the performance of its obligations under the Research Plan during the Research Term. Upon request by Dimension, Bayer shall provide reasonable consulting and technical support in order to assist Dimension in carrying out its Research Program obligations. Bayer shall pay the costs and expenses described in the Research Budget as provided in Section 2.5. To the extent that tasks are allocated to Bayer under the Research Plan, it shall use Commercially Reasonable Efforts in the performance of such tasks.

2.2.2 Notwithstanding the foregoing, (a) to the extent the data from any studies conducted prior to the conduct of the POC Trial, or the requirements of any Regulatory Authority, result in the Parties mutually agreeing, through the JSC, to terminate early the Research Plan (and not to proceed under Section 2.11.2), or (b) where Dimension or Bayer, as the holder of the First IND (as defined in Section 2.13), is required by Regulatory Authorities in the U.S. or E.U. to terminate the further clinical development of all Licensed GT Products (provided that the Parties have exerted Commercially Reasonable Efforts to modify the Research Plan (consistent with Section 2.3.2) to comply with the requirements of Regulatory Authorities), the Parties shall not proceed under Section 2.11.2, and the Research Term will terminate early and the Parties will agree to wind up the conduct of the activities under the Research Plan in an orderly fashion.

2.3 Research Plan, Research Budget, and Operating Plans.

2.3.1 Plans. The overall Research Plan as of the A&R Effective Date is set forth in Exhibit D-1. Within [***] after the Original Effective Date, or longer as agreed by the Parties, the Parties shall develop and finalize a detailed operating plan for carrying out the activities set forth in the Research Plan over the ensuing [***], which such operating plan shall contain the description, time-line and portion of the Research Budget covering such activities (the "Operating Plan"). Such Operating Plan shall be consistent with the terms of this Agreement, the Research Plan and the Research Budget. The Operating Plan as of the A&R Effective Date is attached hereto as Exhibit D-2 and forms a part of this Agreement. In the event of an inconsistency between the Research Plan, Operating Plan and this Agreement, the terms of this Agreement will prevail and in the event of an inconsistency between the Research Plan and

an Operating Plan, the terms of the Research Plan will prevail, unless otherwise agreed in writing by the Parties.

2.3.2 Amendments and Revisions to Operating Plan and Research Plan. During the Research Term, (a) each Party shall provide the JRDC with [***] written reports describing the progress made against the goals set forth in the Operating Plan, and (b) the JRDC shall on a [***] basis review and update the Operating Plan, and make necessary amendments (including any increase in the Research Budget) for the Research Plan activities to be covered in the upcoming [***], consistent with Sections 2.3.3, 2.3.4, and 2.3.5. On a [***] basis, the JRDC shall review and update as needed the then-current Research Plan. Any amendments or modifications to the Research Plan and any Operating Plan shall require the approval of the JRDC (and the JSC, as applicable) and shall be subject to the applicable terms of this Agreement, and the JRDC shall be required to formally document updates to the Research Plan and Operating Plan as part of the agreed upon and accepted minutes of the [***] meetings of the JRDC.

2.3.3 Minor Amendments to the Research Budget. In the course of its [***] review of the Operating Plan, either Party may propose to the JRDC amendments to the then-current annual Research Budget associated with such Operating Plan, to reflect actual costs or minor changes to the Research Plan, and the terms of Section 4.1.4 shall apply to any final decision related to such amendment; provided, however, that if any such proposed amendment to the Research Budget causes the then-current annual Research Budget to increase by more than [***], such amendment to the Research Budget shall require the unanimous approval of the JSC in accordance with Section 2.3.4. Following transfer of the First IND the need for unanimous approval shall no longer apply and Dimension shall not be required to perform any activities without its consent, to be granted or withheld in Dimension's sole discretion.

2.3.4 Major Amendments to the Research Budget. The Parties agree and acknowledge that (a) the Research Budget as of the Original Effective Date represents the good faith estimate of the Parties as to the costs of the activities set forth in the Research Plan, and the extent of activities to be included within the Research Plan itself, (b) subject to Section 2.3.5, such Research Budget is based upon certain assumptions, including but not limited to regulatory requirements, pre-clinical testing, manufacturing requirements, and clinical development activities, as such assumptions are further set forth in Exhibit D-3; and (c) changes to the Research Plan likely will be required where any material changes to such assumptions and/or the activities to be conducted under the Research Plan are agreed upon by the Parties. Accordingly, the Parties agree that any increase to the Research Budget of more than [***] overall (or with respect to any given calendar year), shall require the unanimous approval of the JSC, and that unless and until such approval is obtained (i) [***] shall not be obligated to fund any amount over the expense caps set forth in the then-current agreed upon Research Budget; and (ii) [***] shall not be required to undertake any activities that are not funded fully by the then-current agreed upon Research Budget due to a change in assumptions underlying such activities and their associated costs, or due to any expansion of the scope or nature of any such activity. Following transfer of the First IND the need for unanimous approval shall no longer apply and Dimension shall not be required to perform any activities without its consent, to be granted or withheld in Dimension's sole discretion.

2.3.5 Assumptions in the Research Budget. In addition to any amendments to the Research Budget permitted under Section 2.3.3 or 2.3.4, on [***] basis and through the JRDC, the Parties shall in good faith review the assumptions in the then-current Research Budget and make any appropriate adjustments to such assumptions. Such adjustments by the Parties will at a minimum take into account: any changes in regulatory requirements that may impact clinical development activities, including but not limited to, the number of patients and duration of treatment of the clinical studies set forth in the Research Plan, or the cost per patient; and any unanticipated issues in manufacturing process development. The JRDC shall formally document any such updates to the assumptions in the Research Budget as part of the agreed upon and accepted minutes of the [***] meetings of the JRDC, and shall prepare and approve a revised Research Budget reflecting such agreed upon revised assumptions.

2.3.6 Uncertainty Regarding Certain Costs. The Parties recognize that, notwithstanding Sections 2.3.4 and 2.3.5, significant uncertainty exists as of the Original Effective Date with respect to the good faith estimate and assumptions in the Research Budget regarding costs associated with process transfer and manufacturing of clinical supplies by Dimension's contract manufacturer and the Parties agree to use good faith efforts to manage and provide for such costs including prompt adjustments to the Research Budget as necessary once greater clarity regarding such costs is obtained. The provisions of Section 2.3.4 shall apply if such adjustments result in the Research Budget increasing by more than [***].

2.4 Subcontractors. Dimension may engage any consultant, subcontractor, or other vendor conducting Dimension's obligations under the Research Plan (each, a "Subcontractor") to perform any work under the Research Program; *provided* that all such engagements and any contracts related to such engagements are subject to prior approval by the JRDC, to the extent not already approved as part of and named within the Research Plan or any Operating Plan. Such contracts shall include provisions, including intellectual property provisions, adequate for Bayer to enjoy the licenses granted hereunder as though Dimension had performed the contracted work. To facilitate approval by the JRDC, Dimension shall identify each Subcontractor, the activities proposed to be performed by such Subcontractor and the budget for such activities. The JRDC in its discretion may request a copy of the proposed contract with the Subcontractor prior to approving such contract. Dimension shall be solely responsible for the management of its permitted Subcontractors. Any agreement with a permitted Subcontractor pertaining to the Research Program shall be consistent with the provisions of this Agreement. Dimension shall ensure that no consultant, subcontractor or other vendor it instructs in connection with the Research Plan is or has been debarred by the FDA (or other Regulatory Authority outside the US) pursuant to its authority under Sections 306(a) and (b) of the U.S. Food, Drug, and Cosmetic Act (21 U.S.C. §335(a) and (b)) (or analogous provisions outside the US), or is the subject of any investigation or proceeding which may result in such debarment by the FDA (or other Regulatory Authority in countries outside the US). Bayer may engage a subcontractor in the performance of Bayer's obligations under the Research Plan pursuant to this Section 2.4, *mutatis mutandis*.

2.5 Funding of Research.

2.5.1 Payment to Dimension. [***] Dimension will estimate the total costs and expenses expected to be incurred during such [***] in performing its activities under the

Research Plan, which estimate will be consistent with the applicable Operating Plan and Research Budget. Within [***] following the [***], Dimension will provide Bayer with a report containing an account of tasks actually performed and the costs and expenses actually incurred during such [***] (the "[***] Expense Report"). Such report will specify in reasonable detail all costs and expenses incurred during such [***] and an invoice for such costs and expenses shall accompany the [***] Expense Report. Bayer shall pay such invoices within [***] of their receipt by Bayer.

Invoices will be sent to Bayer at the following address:

Bayer HealthCare
Pharma West Coast
PO Box 416
Pittsburgh PA 15230
USA

2.5.2 Intentionally Omitted.

2.5.3 Cost Overruns. If the Parties determine that Dimension's costs and expenses for [***] in performing its activities under the Research Plan are greater than [*** of the then-current Research Budget for the applicable [***] (such excess over such percentage, a "Cost Overrun"), then Bayer shall have no obligation to pay the Cost Overrun unless Dimension obtains Bayer's consent. If consent is provided, Bayer will pay the excess amount to Dimension; provided, however, if at the conclusion of the Research Plan, the actual amount expended by Bayer, including the Cost Overruns, is greater than the overall cap set forth in the then-current Research Budget, Dimension shall reimburse Bayer the amount of such Cost Overruns in excess of such cap within [***] days of receipt by Dimension of the next Milestone Payment stated in Section 6.2, if such Milestone Event is achieved. The foregoing proviso in the previous sentence shall not apply with respect to the Research Budget or other costs or expenses incurred on or after the A&R Effective Date. For clarity, a Cost Overrun is intended to be an increase to the costs of the Research Plan arising from an oversight or failure on the part of Dimension to budget its activities correctly or efficiently, and not an increase to such costs arising from changes in the nature and scope of activities performed under the Research Plan or changes to the underlying assumptions regarding such activities and their costs, which are addressed under Section 2.3.4. Bayer acknowledges and agrees that, as of the A&R Effective Date, there are no Cost Overruns and that Dimension will not owe any reimbursement to Bayer pursuant to this Section 2.5.3.

2.5.4 Expense Records. Dimension shall maintain complete and accurate books, records and accounts used for the determination of all costs and expenses incurred in connection with the performance of its obligations under the Research Plan and in accordance with the Research Budget, in sufficient detail to confirm the accuracy of any payments required under this Agreement, which books, records and accounts will be retained by Dimension for [***] after creation thereof, or longer as is required by applicable Law. Such books, records and accounts shall be kept in accordance with Dimension's then-current accounting procedures. Bayer shall have the right, during normal business hours and upon reasonable advance notice, to review and copy all such records maintained by Dimension.

2.5.5 Currency. All payments made under this Section 2.5 will be payable in US Dollars.

2.6 Bayer's Expenses. Bayer shall be solely responsible for its own costs and expenses incurred in conducting any activities under the Research Plan or otherwise in support of the Research Program.

2.7 Pre-Clinical and Clinical Supplies. As part of the Research Plan, until transfer of manufacturing responsibilities as defined in the Transition Plan, Dimension shall be responsible for manufacturing or having manufactured sufficient supplies of GT Products and any Compounds/Vectors needed in the conduct of its activities under the Research Plan.

2.8 Regulatory Matters. Unless otherwise agreed by the Parties, Dimension shall be responsible for, and shall compile, submit and shall initially have ownership of, the IND filed by or on behalf of Dimension for any GT Product or component thereof, necessary in order to conduct its activities under the Research Plan. Notwithstanding that Dimension will be the initial holder of the First IND and will transfer all sponsor obligations to Bayer for the POC Trial, Dimension acknowledges that to the extent imposed by applicable Law, for the period of time that Dimension is the holder of the First IND, Dimension will have certain responsibilities for information and support related to the POC Trial and owed to Bayer in Bayer's role as bearing the responsibilities of the sponsor of the POC Trial. Dimension shall provide to Bayer a copy of all written substantive communications from and with any Regulatory Authority involving a regulatory submission for such GT Product or any Compound/Vector or any other component thereof sufficiently in advance, where feasible, to enable Bayer to have a meaningful opportunity to provide input on the content of such submission and, if requested by Bayer, to participate in scientific advice meetings with the Regulatory Authority related to such GT Product. It is intended that at a time mutually agreed upon by the Parties and as described in the Transition Plan, Dimension shall assign and transfer to Bayer, at Bayer's expense, the First IND. Following such assignment and transfer, Bayer shall assume responsibility for communicating and interacting with all Regulatory Authorities. Any orphan designation for the Licensed GT Product and/or the Field for which Dimension has filed or intends to file an IND will be in the name of Bayer or one of its Affiliates.

2.9 Materials. To facilitate the conduct of the Research Plan activities, either Party may provide to the other Party, free of charge, certain biological materials or chemical compounds owned by or licensed to the supplying Party for use by the other Party (such materials or compounds and any progeny and derivatives thereof, collectively, "Materials"). All such Materials shall remain the sole property of the supplying Party, shall be used only in the fulfillment of obligations or exercise of rights under this Agreement and solely under the control of the receiving Party, shall not be used or delivered to or for the benefit of any Third Party without the prior written consent of the supplying Party, and shall not be used in research or testing involving human subjects, unless expressly agreed. Notwithstanding the foregoing, title to all POC Trial Material will pass to Bayer upon delivery of the same, such delivery to occur Ex Works (the facility of the relevant manufacturer). "POC Trial Material" means the GT Product made available by or on behalf of Dimension to Bayer in bulk drug product form for purposes of conducting the POC Trial. Bayer hereby agrees to use the POC Trial Material solely for purposes of conducting the POC Trial and for any additional activities that are relevant to the development

of a Licensed GT Product in accordance with this Agreement. Bayer acknowledges that Bayer will be responsible for secondary packaging, secondary labeling and clinical distribution of the POC Trial Material.

2.10 Research Records and Reports. Each Party shall maintain complete, current and accurate records and laboratory notebooks of all activities it conducts under the Research Program, and all data and other information resulting from such activities. Such records shall reflect all work done and results achieved in the performance of the Research Program in good scientific manner (including in accordance with applicable GLP, GMP and GCP, where appropriate in conformance with the Research Plan) as appropriate for regulatory and patent purposes. Each Party shall have the right, during normal business hours and upon reasonable advance notice, to review and copy all such records maintained by the other Party and to obtain access to the originals in accordance with the terms of the Quality Agreement (as defined below) to the extent necessary or useful for regulatory and patent purposes.

2.11 Licensed GT Products; Demonstration of Clinical POC.

2.11.1 Designation. The Parties intend that during the Research Term and under the Research Plan, the Parties will discover and develop [***] GT Produc[***] and the Parties will coordinate to undertake the POC Trial for [***] GT Product, which [***] GT Product, upon receipt of the POC Data, shall be deemed a "Licensed GT Product," after which point, Bayer's licenses set forth in Section 5.1 (a) and (b) shall apply, and Bayer shall have sole responsibility for further development, manufacture and Commercialization of such Licensed GT Product. For clarity, any POC Trial Material that remains following receipt by a Party of POC Data will be Licensed GT Product and Bayer may use and dispose of the same in accordance with this Agreement.

2.11.2 Failure to Achieve POC. In the event [***] Licensed GT Product is the subject of the POC Trial, but fails to achieve Demonstration of Clinical POC (as determined pursuant to Section 2.11.4), at Bayer's discretion and request, the Parties shall amend the Research Plan and Research Budget to add activities to identify and develop [***] GT Product and conduct a POC Trial for such [***] GT Product (the "Backup Product") and as needed, extend the then-current Research Term to conduct such activities. Such Backup Product, upon Demonstration of Clinical POC, shall also become a Licensed GT Product, subject to the license grants set forth in Section 5.1, and the Parties shall determine if such Backup Product achieves Demonstration of Clinical POC pursuant to Section 2.11.4.

2.11.3 Follow On Products. If notwithstanding Demonstration of Clinical POC for the [***] Licensed GT Product or a Backup Product, Bayer requests, at any time prior to Bayer's submission of the first MAA for a Licensed GT Product, that an additional GT Product also be identified and made the subject of an additional POC Trial, the Parties shall discuss in good faith such request, and if mutually agreed, shall either modify the then-current Research Plan and Research Budget to include such activities or (if no Research Plan remains in place) agree a new Research Plan and Research Budget, and [***], and as necessary the Parties shall extend the Research Term or reinstate a Research Term to accommodate such activities, and any such additional GT Product as to which such an additional POC Trial is conducted

would be deemed also a Licensed GT Product and subject to Bayer's license grants set forth in Section 5.1.

2.11.4 Determination of Demonstration of Clinical POC. The process for determining achievement of Demonstration of Clinical POC for a Licensed GT Product shall be as set forth in this Section 2.11.4. Following receipt by a Party of POC Data for the Licensed GT Product, Bayer will present the results of such trial, and all other relevant data, to the JSC and the JSC will act in good faith to apply the criteria set forth in Exhibit E to such data and results and determine if such criteria for Demonstration of Clinical POC have been met. If the JSC determines that such criteria have been met, then Demonstration of Clinical POC will be deemed to have been achieved and Dimension will invoice Bayer for the applicable milestone payment as set forth and in accordance with Section 6.2. If the JSC determines that such criteria in Exhibit E have not been met with respect to the initial Licensed GT Product then the Parties may proceed in accordance with Section 2.11.2. In the event of any disagreement within the JSC on the application of the criteria set forth in Exhibit E, and/or whether Demonstration of Clinical POC has been achieved, the Parties shall within [***] of the meeting of the JSC in which it was unable to so determine such achievement, identify and appoint a mutually agreed upon independent industry expert (the "Expert"). In such case, each Party shall provide the Expert with the relevant data as well as a briefing document setting forth specific detailed reasons underlying such Party's position, and the Expert shall within an additional [***] following his appointment, apply the criteria and make the determination, in a writing stating his reasons for such position, of whether Demonstration of Clinical POC has been achieved, which determination shall be final and binding on the Parties. All costs associated with identifying and utilizing such Expert shall be borne equally by the Parties. Following a positive determination by the Expert that Demonstration of Clinical POC has been achieved, Dimension will invoice Bayer for the applicable milestone payment as set forth and in accordance with Section 6.2. For the avoidance of doubt, in determining the achievement of Demonstration of Clinical POC hereunder, either by the JSC or the Expert, the criteria stated in Exhibit E shall be strictly applied and shall not be modified in any way. No opinion as to materiality or relevance of any of the results or data (including their applicability to any particular patient) shall replace or modify the specific figures and other criteria expressly stated in Exhibit E. Furthermore, the Expert shall make his decision based on the data and briefing documents submitted to him. If he is unable to make a decision without additional information or data, Demonstration of Clinical POC will be deemed not to have been achieved.

2.12 Transition Plan. Without limiting Dimension's obligations under any agreement reached by the Parties pursuant to Section 3.4, each Party will conduct the activities allocated to it in the Transition Plan. For the avoidance of doubt, Dimension shall, [***], in accordance with the Transition Plan, conduct all necessary technology transfer (including Materials) to Bayer as reasonably necessary for Bayer to practice the licenses granted under Section 5.1 with respect to such Licensed GT Product.

2.13 First IND. "First IND" means IND # 18124 submitted by or on behalf of Dimension to the FDA on or about April 12, 2018, as may be amended from time to time.

2.14 Amendment and Restatement. The Parties hereby acknowledge and agree that this Agreement amends and restates the Original Agreement in its entirety and the Original

Agreement is replaced with and superseded by, this Agreement. Any activities conducted under the Original Agreement shall be deemed to have been conducted under this Agreement.

ARTICLE 3: LATER STAGE DEVELOPMENT AND COMMERCIALIZATION

3.1 General Responsibilities. Following completion of the Transition Plan and except as otherwise agreed by the Parties pursuant to Section 3.4, Bayer shall be solely responsible for (i) the planning and conduct of all later development of such GT Product or Licensed GT Product in the Field in the Territory, (ii) all regulatory submissions and approvals (including all INDs and MAAs) for such GT Product or Licensed GT Product and interactions with regulatory authorities, (iii) the selection of the countries in the Territory in which Bayer will pursue and maintain Regulatory Approvals, including at a minimum the U.S. and at least [***] Major Market Countr[***]; and (iv) Commercialization of such Licensed GT Product in the Territory, all at its sole expense.

3.2 Development Activities.

3.2.1 Bayer's Efforts. Bayer, itself or through one or more Affiliates or Sublicensees, shall use Commercially Reasonable Efforts to conduct and complete the POC Trial, conduct a Pivotal Trial and such other clinical development activities as are required to obtain Regulatory Approval in the U.S. and at least [***] Major Market Countr[***] in the Territory for the Licensed GT Product. Bayer shall ensure that no consultant, subcontractor or other vendor it instructs in connection with such development is or has been debarred by the FDA (or other Regulatory Authority outside the U.S.) pursuant to its authority under Sections 306(a) and (b) of the U.S. Food, Drug, and Cosmetic Act (21 U.S.C. §335(a) and (b)) (or analogous provisions outside the U.S.), or is the subject of any investigation or proceeding which may result in such debarment by the FDA (or other Regulatory Authority in countries outside the U.S.).

3.2.2 Regulatory Submissions and Approvals. Bayer shall be solely (except as stated in Exhibit D-4) responsible for filing for and shall own all Regulatory Approvals and submissions therefor. To the extent permitted by applicable Laws, Bayer shall permit Dimension to attend in an observatory capacity only all meetings with Regulatory Authorities in the U.S., to the extent related to a GT Product or Licensed GT Product, including, but not limited to, all in-person meetings and all telephone conferences.

3.2.3 Updates. Bayer shall update the JSC on its progress with respect to obtaining Regulatory Approval of the GT Product or Licensed GT Product, including providing to the JSC in advance of its meeting a written summary (which may be in presentation style) that includes sufficient detail for Dimension's representatives to understand the activities planned by Bayer and Bayer's anticipated timelines for performing such activities, and any material interactions with Regulatory Authorities. In addition, each Party shall immediately notify the other of any information it receives regarding any threatened or pending action, inspection or communication by or from any Third Party, including a Regulatory Authority, that may materially affect the development, manufacturing, Commercialization or regulatory status of a GT Product or Licensed GT Product.

3.2.4 PV Agreement. If requested by Bayer the Parties will enter into an Agreement setting forth the specific procedures to be used by the Parties to coordinate the investigation and exchange of reports of adverse drug experiences and product complaints with respect to Licensed GT Products to ensure timely communication to Regulatory Authorities and compliance with Laws.

3.3 Commercialization.

3.3.1 Responsibilities. Bayer will have the exclusive right to conduct, and be solely responsible for, all aspects of the Commercialization of Licensed GT Products in the Field in the Territory, including: (a) developing and executing a commercial launch and pre-launch plan, (b) negotiating with applicable governmental authorities regarding the price and reimbursement status of Licensed GT Products; (c) marketing and promotion; (d) booking sales and distribution and performance of related services; (e) handling all aspects of order processing, invoicing and collection, inventory and receivables; and (f) providing customer support, including handling medical queries, and performing other related functions. As between the Parties, Bayer shall bear all of its costs and expenses incurred in connection with such Commercialization activities.

3.3.2 Compliance. Bayer shall be responsible for conforming its practices and procedures to applicable Laws relating to the marketing, detailing and promotion of Licensed GT Products and/or Licensed Treatments in the Territory.

3.4 Manufacturing Assistance. Following delivery of the POC Trial Material in accordance with the Transition Plan and that certain Quality Agreement entered into by and between the Parties or any of their Affiliates, dated on or about April 25, 2018 (the "Quality Agreement"), Bayer shall be responsible for the manufacture of the Licensed GT Products for clinical or commercial use, including any process development and scale up. Notwithstanding the foregoing, Dimension shall provide the support outlined in Exhibit D-4, and shall negotiate in good faith an agreement to provide reasonable additional support and assistance as Bayer might consider to be necessary in connection with the manufacturing process. Dimension shall not be obligated to provide any such additional support prior to the Parties entering into a written agreement with respect to the same, which shall provide for reasonable compensation to be paid.

ARTICLE 4: GOVERNANCE

4.1 Joint Steering Committee.

4.1.1 Formation and Dissolution. The JSC shall be formed as soon as possible, but no later than [***] following the Original Effective Date of this Agreement and, unless otherwise agreed by the Parties, shall dissolve at the time of initial Regulatory Approval in the U.S., or earlier should Dimension elect to discontinue the JSC following Demonstration of Clinical POC. The JSC shall be comprised of [***] representatives from each Party. If mutually agreed by the JSC members on a case-by-case basis, the JSC may invite other non-members to participate in the discussions and meetings of the JSC, provided that such participants shall have no voting authority at the JSC. Each Party may substitute its representative from time-to-time

effective only upon the consent of the other Party, not to be unreasonably withheld. The JSC shall have no permanent chairman.

4.1.2 Responsibilities. The JSC shall be responsible for overseeing the overall collaboration established under this Agreement, and to that end, for (i) creating and maintaining a collaborative work environment within and among the Parties, and (ii) addressing any disputes as they may arise in the JRDC and (iii) determining whether Demonstration of Clinical POC has been achieved, and (iv) unless otherwise specified, serving as the initial point of contact to resolve any disputes between the Parties. The JSC will have solely the powers assigned to it in this Article 4 and elsewhere expressly in this Agreement, and will not have any power to amend, modify, or waive compliance with this Agreement.

4.1.3 Meetings. The JSC shall meet in person or by teleconference not less than [***] during the Research Term, and thereafter, once every [***] until dissolution. Meetings of the JSC shall be alternately hosted by the Parties on such dates and at such times, places and format (i.e. whether the meeting will be in person or by teleconference) as agreed to by the members of the JSC; *provided*, that at least one meeting in each calendar year during the Research Term shall be in person. Dimension shall host the first meeting of the JSC at a mutually agreeable time and place no later than [***] from the Original Effective Date of this Agreement. Each Party shall be responsible for all its own expenses relating to attendance at or participation in JSC meetings. The representatives shall alternate acting as chairman of each meeting, and in that capacity shall be responsible for sending out in advance the agenda for any such meeting and minuting the results of such meeting for review and approval within [***] after each JSC meeting. Such minutes shall be deemed approved unless one or more members of the JSC objects to the accuracy of such minutes within [***] of receipt. For the avoidance of doubt, the chairman shall have no casting vote. Meetings of the JSC shall be effective only if at least one (1) representative of each Party is present or participating in such meeting.

4.1.4 Decision-Making. The JSC will strive to reach consensus in all decisions before it. The representative from each Party will have one (1) vote on behalf of that Party. The representatives serving on the JSC shall use good faith efforts to seek consensus in the JSC's decision making process and to make decisions that are consistent with the then existing Operating Plan and Research Plan. In the event such consensus is not obtained within [***] of the JSC reviewing and discussing an issue, subject in all events to Sections 2.3.3 and 2.3.4, (a) until transfer of the First IND to Bayer, Dimension's representative shall have final say with respect to any decision involving any amendment to, or the conduct of any activities under, the Research Plan, Research Budget, or any Operating Plan; provided that Dimension's representatives shall not have the right in the exercise of such final say to amend, revise or extend the Research Plan or Research Budget in a manner that (i) changes the primary and secondary endpoints of the POC Trial; (ii) imposes any material additional obligations on Bayer or (iii) results in any Cost Overrun or increases the overall Research Budget by more than [***] of the then-current Research Budget; and (b) following transfer of the First IND to Bayer, [***] representative shall have the final say with respect to any decision involving development activities as outlined in Section 3.2, or Commercialization as outlined in Section 3.3, or any manufacture of Licensed GT Products. For clarity, the determination of whether Demonstration of Clinical POC has been achieved for a Licensed GT Product will be in accordance with Section 2.11.4. Following Demonstration of Clinical POC the JSC will function primarily as an

information exchange forum and the existence of the JSC and Bayer's participation therein does not affect any decision-making discretion or right that Bayer otherwise possesses under this Agreement.

4.2 Joint Research and Development Committee.

4.2.1 Formation. The Parties shall form a Joint Research and Development Committee as soon as possible after the Original Effective Date, but no later than [***] following the Original Effective Date of this Agreement. The JRDC shall be comprised of an equal number of representatives from each Party. If mutually agreed by all JRDC members, the JRDC may invite non-members (including ReGenX personnel) to participate in the discussions and meetings of the JRDC, provided that such participants shall have no voting authority at the JRDC. Each Party shall notify the other Party in writing of its initial representatives to the JRDC within [***] after the Original Effective Date, and may substitute one or more representatives from time-to-time effective upon written notice to the other Party, provided that such representatives are suitably qualified and experienced for the tasks and responsibilities to be fulfilled. A designated representative of Dimension will be the chairman of the JRDC, and in such capacity, he/she shall be responsible for setting the agenda for meetings of the JRDC, with input from the other members, and for conducting the meetings of the JRDC. Except as stated above the chairman will have no casting vote.

4.2.2 Responsibilities. The JRDC shall be responsible for oversight of the conduct of research and development under the Research Plan during the Research Term. In addition to the foregoing general responsibilities, the JRDC shall in particular:

(a) Review, discuss and approve any proposed Operating Plan or the Research Budget and timelines in the Research Plan and under each Operating Plan, or amendments thereto,

(b) manage the overall strategy for the research and development of potential Licensed GT Products under the Research Plan,

(c) prioritize GT Products for further research and development under the Research Plan,

(d) determine criteria to be set forth in the Research Plan for selection of a development candidate with respect to a GT Product, and whether such criteria have been met,

(e) make decisions on whether and how to continue activities under the Research Plan at each decision point set forth in such Research Plan, based on the then-available data and results and consistent with the criteria set forth in such Research Plan,

(f) oversee Dimension's efforts to obtain any and all requisite INDs with respect to any development candidate GT Products,

(g) perform such other functions as appropriate to further the purposes of the Research Program, as expressly set forth in this Agreement or as determined by the Parties in writing,

(h) be responsible for ensuring the submission of clinical trial information by the sponsor of the POC Trial to the relevant public databases (e.g. ClinicalTrials.gov) when legally required and ensuring consistency between all postings. In addition (and at a minimum), the JRDC will ensure compliance with the requirements of the latest version of "Joint Position on the Disclosure of Clinical Trial Information via Clinical Trial Registries and Databases" as defined by IPFMA, PhRMA, EFPIA, and JAMA will be followed for all trials globally; and

(i) agree on a publication strategy based on the Parties' normal practices and policies.

The JRDC will have solely the powers assigned to it in this Article 4 and elsewhere expressly in this Agreement, and will not have any power to amend, modify, or waive compliance with this Agreement.

4.2.3 Meetings. The JRDC shall meet at least [***] per Calendar Quarter, unless the Parties mutually agree in writing to a different frequency for such meetings. Either Party may also call a special meeting of the JRDC (by videoconference or teleconference) by at least [***] prior written notice to the other Party in the event such Party reasonably believes that a significant matter must be addressed prior to the next regularly scheduled meeting, and such Party shall provide the JRDC, no later than [***] prior to the special meeting, with materials reasonably adequate to enable an informed decision. No later than [***] prior to any meeting of the JRDC, the chairperson of the JRDC shall prepare and circulate an agenda for such meeting; provided, however, that either Party may propose additional topics to be included on such agenda, either prior to or in the course of such meeting. The JRDC may meet in person, by videoconference or by teleconference, provided, however, at least [***] shall be in person unless the Parties mutually agree in writing to waive such requirement in lieu of a videoconference or teleconference. In-person JRDC meetings shall be held at locations alternately selected by Dimension and by Bayer. Each Party shall bear the expense of its respective JRDC members' participation in JRDC meetings. Meetings of the JRDC shall be effective only if at least one (1) representative of each Party is present or participating in such meeting. The chairperson of the JRDC shall be responsible for preparing reasonably detailed written minutes of all JRDC meetings that reflect, without limitation, all material decisions made at such meetings. The JRDC chairperson shall send draft meeting minutes to each member of the JRDC for review and approval within [***] after each JRDC meeting. Such minutes shall be deemed approved unless one or more members of the JRDC objects to the accuracy of such minutes within [***] of receipt.

4.2.4 Decision-Making. The JRDC will strive to reach consensus in all decisions before it. The representatives from each Party will have, collectively, one (1) vote on behalf of that Party. The representatives serving on the JRDC shall use good faith efforts to seek consensus in the JRDC's decision making process. In the event such consensus is not obtained within [***] of the JRDC reviewing and discussing an issue, the matter may be referred by either

Party to the JSC for resolution, in which forum, until transfer of the First IND to Bayer, Dimension's representatives to the JSC shall have the final say with respect to such decision or dispute; provided that Dimension's representatives shall not have the right in the exercise of such final say to amend, revise or extend the Research Plan in a manner that (i) imposes any material additional obligations on [***] or (ii) results in any Cost Overrun. Following transfer of the First IND to Bayer, subject in all events to Sections 2.3.3 and 2.3.4, [***] representative shall have the final say with respect to such decision or dispute.

4.2.5 Discontinuation of the JRDC. The JRDC shall continue to exist until the first to occur of (a) expiration of the Research Term, or (b) the Parties mutually agreeing to disband the JRDC. After the JRDC is disbanded, any decisions previously within its purview shall be decisions between the Parties, but governed by the decision making rules set forth in Section 4.2.4 as they apply to a Party's representatives on the JRDC.

4.3 Joint Project Team. Within [***] following dissolution of the JSC, the Parties agree to form a joint project team (the "Joint Project Team" or "JPT"). The JPT's purpose will be to facilitate the exchange of information with respect to (a) the commercialization, including reimbursement strategies, regarding the Licensed GT Product and Licensed Treatment and Dimension's gene therapy products, in particular, in the field of Hemophilia B, and (b) the continued clinical development of the Licensed GT Product post Regulatory Approval. The JPT shall meet at least [***] either telephonically or in person, unless the Parties mutually agree in writing to a different frequency for such meetings. For clarity, the JPT functions primarily as an information exchange forum and does not affect any decision-making discretion or right that Bayer otherwise possesses under this Agreement.

4.4 Alliance Manager. Each of Dimension and Bayer shall appoint a representative who possesses a general understanding of clinical, regulatory, manufacturing and marketing issues to act as its Alliance Manager ("Alliance Manager"). Each Alliance Manager will be responsible for:

(a) coordinating the various functional activities of Dimension and Bayer, as described in this Agreement;

(b) providing single-point communication for seeking consensus both within the respective Party's organization and with the other Party's organization regarding key issues, as appropriate, including facilitating review of external corporate communications; and

(c) identifying and raising cross-Party and/or cross-functional disputes to the appropriate committee or management in a timely manner.

ARTICLE 5: LICENSE GRANT; EXCLUSIVITY; NEGOTIATION RIGHTS

5.1 License Grant. Subject to the terms and conditions of this Agreement, including the Retained Rights, Dimension hereby grants to Bayer (a) an exclusive (even as to Dimension), sublicensable (as provided in Section 5.6 only), non-transferable (except as provided in Section 13.2), royalty-bearing license, under the Licensed Technology to make, have made, use, administer, monitor, import, sell, and offer for sale Licensed GT Products and Licensed

Treatments, solely in the Field; (b) a non-exclusive, sublicenseable, non-transferable (except as provided in Section 13.2), [***] license under the Dimension Manufacturing Patents to manufacture or have manufactured (i) the GT Product that comprises the POC Trial Material, solely for purposes of conducting subsequent clinical trials of such GT Product, (ii) the Licensed GT Product, (iii) Licensed Treatment and/or (iv) any Compound/Vector used therein, in each case ((i)-(iv)), solely in the Field; and (c) a non-exclusive, non-sublicenseable, non-transferable (except as provided in Section 13.2), [***] license under the Dimension POC Technology to use the POC Trial Material solely to conduct the POC Trial and as permitted pursuant to Section 2.9. "Dimension POC Technology" means (i) all Patent Rights that (A) are not Sublicensed Patents, (B) are not Dimension Manufacturing Patents, (C) are owned or Controlled by Dimension or its Controlled Affiliates as of the A&R Effective Date or that come into the ownership or Control of Dimension or its Controlled Affiliates after the A&R Amendment Effective Date and prior to the completion of the POC Trial (other than through the grant of a license by Bayer hereunder), and (D) cover the use of the POC Trial Material in the POC Trial and (ii) any Know-How that (A) is Controlled by Dimension or any of its Controlled Affiliates as of the A&R Amendment Effective Date or comes into the Control of Dimension or any of its Controlled Affiliates after the A&R Amendment Effective Date and prior to the completion of the POC Trial (other than through the grant of a license by Bayer hereunder), (B) is reasonably necessary or useful for the use of the POC Trial Material in the POC Trial and as permitted pursuant to Section 2.9, and (C) is neither (i) Sublicensed Know-How, nor (ii) any Manufacturing Technology which is other than [***] Know-How, and that comes into the Control of Dimension under the ReGenX Agreement or another agreement with ReGenX.

5.2 Upstream Retained Rights for Hemophilia A. Notwithstanding the licenses granted in Section 5.1, Bayer acknowledges and agrees that, ReGenX's direct and indirect licensors retain the following rights: to the extent any Sublicensed Technology pertains to recombinant adeno-associated virus serotype 8, an exclusive, sublicensable right to make, have made, use, sell, offer for sale, and import products for the treatment of hemophilia A.

5.3 Other Retained Rights. Except for the rights and licenses specified in Section 5.1, no license or other rights are granted to Bayer under any intellectual property of Dimension or ReGenX, whether by implication, estoppel, or otherwise, whether, in the case of ReGenX, any such intellectual property dominates or is dominated by the Licensed Technology or Dimension POC Technology. Notwithstanding anything to the contrary in this Agreement, Dimension may use and permit others to use the Licensed Technology for any research, development, commercial, or other purposes, outside of the Field. Dimension shall use reasonable efforts and impose conditions on any of its licensees to whom it grants rights under the Licensed Technology outside the Field to prevent use (intentional or unintentional) of the Licensed Technology inside the Field. Without limiting the foregoing, and notwithstanding anything in this Agreement to the contrary, Bayer acknowledges and understands that ReGenX and its direct and indirect licensors retain the rights under the Sublicensed Technology set forth in Exhibit C (individually and collectively, the "Retained Rights").

5.4 Regained Rights. The Parties acknowledge that the Retained Rights with respect to hemophilia A set forth in Section 5.2 are excluded from this Agreement because of currently existing rights granted by ReGenX to other licensees or Third Parties. If ReGenX (and subsequently Dimension, pursuant to the ReGenX Agreement) regains the rights described in

Section 5.2, following Dimension's receipt of notification from ReGenX of such event, Dimension will notify Bayer of same, together with a description of the rights granted or regained, in which case, such rights will no longer be considered Retained Rights, and the license granted to Bayer under Section 5.1 (a) with respect to Sublicensed Technology will no longer be subject to such Retained Rights.

5.5 Government Rights. Bayer acknowledges that, pursuant to Title 35 of the United States Code, Sections 200–204, the United States government may retain certain rights in intellectual property contained within the Sublicensed Technology if it has been funded in whole or part under any contract, grant, or similar agreement with a federal agency. The license grant hereunder is expressly subject to any applicable United States government rights, including any applicable requirement that products resulting from such intellectual property sold in the United States must be substantially manufactured in the United States absent, with respect to such manufacturing requirement, a waiver of such requirement obtained from the applicable governmental agency. At Bayer's request Dimension will assist Bayer and provide necessary documentation and support in order to obtain such a waiver.

5.6 Sublicensing.

5.6.1 Right to Sublicense. The licenses granted pursuant to Section 5.1 are sublicensable (a) by Bayer to any Affiliates without prior consent by Dimension, or (b) by Bayer to any Third Parties upon Dimension's prior written consent (such consent not to be unreasonably withheld); provided that any such sublicense (to an Affiliate or to a Third Party) must comply with the provisions of this Section 5.6 (including Section 5.6.2). The use, marketing and sale of Licensed Treatment by Bayer's Affiliates shall be deemed to be use, marketing and sale by Bayer and shall not require a sublicense.

5.6.2 Conditions. The right to sublicense granted to Bayer under this Agreement is subject to the following conditions as they relate to sublicenses of the Sublicensed Technology:

(a) Bayer may only grant sublicenses to Third Parties through multiple tiers pursuant to a written sublicense agreement with the Sublicensee. Dimension must receive written notice as soon as practicable following execution of any such sublicenses with Third Parties.

(b) In each sublicense agreement, the Sublicensee must be required to comply with the terms and conditions of this Agreement to the same extent as Bayer has agreed and, in each sublicense agreement with a Third Party, must acknowledge that ReGenX is an express third party beneficiary of such terms and conditions under such sublicense agreement; provided that nothing shall prevent Bayer from granting sublicenses of more limited scope than Bayer's rights, *e.g.*, in a more limited territory, field of use, or term.

(c) The official language of any sublicense agreement with a Third Party shall be English.

(d) Within [***] after entering into a sublicense with a Third Party, Dimension must receive a copy of the sublicense written in the English language for

Dimension's records and to share with ReGenX and its licensors under the Existing Licenses. The copy of the sublicense may be redacted to exclude confidential information of the applicable Sublicensee or of Bayer to the extent not relevant to Dimension or ReGenX, but such copy shall not be redacted to the extent that it impairs Dimension's (or ReGenX's or any of its licensors') ability to ensure compliance with this Agreement.

(e) With respect to sublicense agreements with Affiliates, Bayer shall notify Dimension of the identity of all such Affiliates to which a sublicense is granted, and upon any request of ReGenX, shall provide to ReGenX a copy of such sublicense, in English, within [***], for ReGenX to send GSK and UPenn.

(f) Notwithstanding subsections (d) and (e) above, Bayer acknowledges and agrees that in the event any of ReGenX's licensors under the Existing Licenses have a contractual right to require, and do require, a complete, unredacted copy of Bayer's sublicense agreement granted under this Section 5.6, then Bayer will provide such complete, unredacted copy.

5.6.3 Bayer's execution of a sublicense agreement will not relieve Bayer of any of its obligations under this Agreement. Bayer is and shall remain primarily liable to Dimension for all of Bayer's duties and obligations contained in this Agreement and for any act or omission of an Affiliate or Sublicensee that would be a breach of this Agreement if performed or omitted by Bayer, and Bayer will be deemed to be in breach of this Agreement as a result of such act or omission.

5.7 Bayer's Improvements.

5.7.1 Grant Back. Bayer hereby grants to Dimension a non-exclusive, worldwide, [***], transferable, sublicensable, irrevocable, perpetual license:

(a) to use any Licensed Back Improvements (and any intellectual property rights with respect thereto) consummate in scope to the Retained Rights; and

(b) to practice the Licensed Back Improvements (and any intellectual property rights with respect thereto) in connection with any recombinant adeno-associated virus vectors, including the right to research, develop, make, have made, use, offer for sale, and sell products and services; provided that, during the term of this Agreement, Dimension and its sublicensees shall have no right under the license in this Section 5.7.1b) to practice the Licensed Back Improvements in the Field except as necessary to carry out Dimension's obligations hereunder.

5.7.2 Notice. Bayer agrees to provide prompt notice to Dimension upon the filing of any patent application covering any Licensed Back Improvement, together with a reasonably detailed description of or access to such Licensed Back Improvement to permit the practice of any such invention or improvement.

5.8 ReGenX Improvements. Dimension agrees to provide notice to Bayer promptly following receipt of notice from ReGenX of the filing of any patent application covering any

ReGenX Improvement, together with such description of or access to such ReGenX Improvement as is received by Dimension from ReGenX to permit the practice of any such improvement. Upon Dimension's receipt of notice from ReGenX of the filing of any patent application covering any ReGenX Improvement, Sublicensed Patents in Exhibit A attached hereto will be modified to add such patent application.

5.9 Covenants Related to ReGenX Agreement. During the term of this Agreement, without the prior written consent of Bayer Dimension agrees not to exercise its right to terminate and will not amend the ReGenX Agreement if such termination or amendment would materially or adversely alter the rights of Bayer under this Agreement. In addition, Dimension agrees that it shall not agree to any exercise by ReGenX of its right to terminate the Existing Licenses without first consulting with and obtaining the consent of, Bayer, except to the extent any such termination is in part and relates only to Sublicensed Technology uses outside the Field [***].

5.10 Third Party Beneficiary. Bayer agrees and acknowledges that ReGenX is an express third party beneficiary of the terms and conditions of this Agreement as they relate to the terms and conditions of the ReGenX Agreement.

5.11 Exclusivity.

5.11.1 Dimension. Dimension hereby covenants that Dimension shall not, alone or in collaboration with a Third Party, (a) during the Research Term conduct clinical development of, and (b) during the term of this Agreement Commercialize, [***], other than the Compounds/Vectors, GT Products and Licensed GT Products in accordance with the provisions of this Agreement.

5.11.2 Bayer. Bayer hereby covenants that (a) during the term of this Agreement, and (b) for a period of [***] after termination of this Agreement if terminated by Bayer for convenience pursuant to Section 9.2, Bayer and its Affiliates, either on their own or in collaboration with a Third Party, shall not conduct clinical development of or Commercialize any [***], other than the Licensed GT Products or any Compound/Vector used therein under this Agreement.

5.12 Hemophilia B Program.

5.12.1 Dimension's Rights. Bayer acknowledges and understands that Dimension intends to develop and, if successful, Commercialize one or more gene therapy treatments for hemophilia B utilizing the Sublicensed Technology (the "Hemophilia B Program"). Subject to Dimension's obligations under Sections 5.12.2 and 5.12.3, as between the Parties, Dimension shall have all rights, and be solely responsible for [***], to (i) pursue any such development or Commercialization activities with respect to such Hemophilia B Program and any products arising therefrom, (ii) enter into any licensing, asset sale, distribution, collaboration or other similar arrangements with any Third Party with respect to such Hemophilia B Program, or (iii) elect to terminate and not pursue any such Hemophilia B Program and revert such rights, as and to the extent required, to ReGenX pursuant to the ReGenX Agreement.

5.12.2 Right of First Notice. If, during the period commencing on [***] and ending on the [***] ("Notice Period"), Dimension elects for the first time to enter into discussions with a Third Party for rights to develop and Commercialize (or just to Commercialize) products arising out of its Hemophilia B Program in any country of the Territory, Dimension shall provide Bayer with [***], and Bayer will have a period of [***] in which to inform Dimension of its potential interest in negotiating for such rights (the "Expression of Interest Notice"). Dimension shall review any such Expression of Interest Notice [***], and [***]. Nothing in this Section 5.12.2 shall obligate Dimension or Bayer to enter into any license or other arrangement with respect to the Hemophilia B Program. For clarity, Dimension's obligation to provide written notice to Bayer under this Section 5.12.2 shall only apply [***]. The Parties hereby acknowledge and agree that Dimension fulfilled its obligations under this Section 5.12.2 with respect to the entire world prior to the A&R Effective Date.

5.12.3 Rights Post POC Trial. If, after [***], Bayer desires to enter into negotiations with Dimension with respect to obtaining rights to develop and Commercialize products arising out of its Hemophilia B Program in any country of the Territory, it shall have the one-time right to so notify Dimension in writing, and upon receipt of such notice Dimension shall, within [***], notify Bayer in writing whether and to what extent Dimension still retains such rights to the Hemophilia B Program in the Territory (the "Availability Notice"), and upon receipt of such Availability Notice, Bayer may elect to deliver to Dimension, within [***], a notice of its interest in entering into negotiations with Dimension for a license to such then-remaining rights held by Dimension (the "Negotiation Notice"). Upon receipt of such Negotiation Notice, Dimension and Bayer shall negotiate in good faith the terms of such a potential license agreement for such then-remaining rights, for a period of [***] (or longer or fewer, to the extent the Parties agree to extend or terminate such discussions mutually) a term sheet or letter of intent with the level of detail similar to that of the term sheet exchanged between the Parties with respect to this Agreement and the Licensed GT Products, and Dimension shall not enter into any license or other arrangement with a Third Party for such rights until the lapse of such [***] period. Nothing in this Section 5.12.3 shall obligate Dimension or Bayer to enter into any license or other arrangement with respect to the Hemophilia B Program.

5.12.4 Consultation. Without limiting Sections 5.12.2 and 5.12.3, the Parties agree to consult with one another within the JSC and the JPT, and to the extent they determine, each in its sole discretion and to the extent allowed by applicable Law, that coordinating and communicating to one another with respect to their development, regulatory and Commercialization activities in the Field and in the field of hemophilia B gene therapy treatments, would be likely to have a positive impact on the advancement of the regulatory pathway and Commercialization of gene therapy treatments for hemophilia generally.

ARTICLE 6: CONSIDERATION

6.1 License Fee. In consideration of the licenses granted to Bayer under Section 5.1, Bayer shall pay to Dimension a non-refundable, non-creditable license fee of Twenty Million Dollars ($20,000,000) within [***] of receipt of an invoice therefor, which such invoice may be delivered to Bayer on or after the Original Effective Date.

6.2 Development and Commercial Milestone Payments. Bayer shall make the following one-time development milestone payments to Dimension in connection with the first achievement by Bayer or its Affiliates or Sublicensees of the following development and commercial events. Bayer shall pay to Dimension the applicable amount within [***] of receipt of an invoice issued no earlier than the date of such achievement. Dimension shall provide written notice to Bayer of the occurrence of any of the [***] milestones set forth below, and Bayer shall provide written notice to Dimension of the occurrence of any of the [***] milestones, in each case no later than [***] following the occurrence of the relevant milestone. The [***] milestone, "[***]," shall be determined as set forth in Section 2.11.4.

No.	Development Milestone Event	Milestone Payment
1	[***]	Five Million Dollars ($5,000,000)
2	[***]	Ten Million Dollars ($10,000,000)
3	[***]	[***] Dollars
4	[***]	[***] Dollars
5	[***]	[***] Dollars
6	[***]	[***] Dollars
7	[***]	[***] Dollars
8	[***]	[***] Dollars
	Total	[***] Dollars

Each milestone payment is payable [***] Dollars, regardless of the number of times the corresponding event is achieved by a Licensed GT Product and/or Licensed Treatment and regardless of the number of Licensed GT Products and/or Licensed Treatments to achieve such event. Under no circumstances shall Bayer be obligated to pay Dimension more than [***] Dollars [***] Dollars pursuant to this Section 6.2.

For the avoidance of doubt, the Parties acknowledge and agree that, (a) with respect to Milestone [***] above, in the event that some but not all of the criteria for [***] are met for a Licensed GT Product and/or Licensed Treatment, such that there is no current achievement of [***] as defined, then to the extent the subsequent milestone event (i.e., Milestone [***]) is achieved at a later date for such Licensed GT Product and/or Licensed Treatment, [***] shall be deemed to have occurred at such later date and the corresponding milestone payments for both Milestone [***] and Milestone [***] shall be paid together; and (b) if [***], then all development milestone events relating to [***] shall be deemed to have been met. To that end, if

for any reason, any such related milestone payments have not been made, such milestone payments shall be due and owing upon [***]. For example: if [***] and any of Milestone Events [***] or [***] have not been paid for any reason, all such unpaid milestones shall be paid together with the payment of the milestone payment for the achievement of development Milestone Event [***].

6.3 Sales Milestones. Bayer shall make the following one-time sales milestone payments to Dimension when the aggregate annual Net Sales of all Licensed Treatments in all countries in the Territory by Bayer and its Affiliates and Sublicensees in a calendar year first reach the amount specified below. Bayer shall pay to Dimension such amount within [***] following receipt of an invoice issued no earlier than the date of Bayer's notice of such achievement. Bayer shall provide written notice to Dimension within [***] in which such event is achieved for the first time.

Sales Milestone Event	**Milestone Payment**
[***]	[***]
[***]	[***]
[***]	[***]
Total	[***]

Under no circumstances shall Bayer be obligated to pay Dimension more than [***] pursuant to this Section 6.3. For the avoidance of doubt, more than one of the foregoing milestones with respect to the relevant aggregate Net Sales may occur in any given calendar year. For illustrative purposes only, [***].

6.4 Royalties.

6.4.1 Royalty Rates. Bayer shall pay to Dimension during the Royalty Term royalties on aggregate annual Net Sales of all Licensed Treatments in the Field in the Territory, as calculated by multiplying the applicable royalty rate below by the corresponding amount of incremental Net Sales of all such Licensed Treatments in the Territory in each calendar year:

Aggregate Annual Net Sales	**Royalty Percentage**
[***]	[***]%
[***]	[***]%
[***]	[***]%

6.4.2 Royalty Term. Bayer's obligation hereunder for payment of a royalty under this Section 6.4 on the Net Sales of Licensed Treatments in a given country will

commence on the First Commercial Sale of such Licensed Treatment, and end on a Licensed Treatment-by-Licensed Treatment and country-by-country basis upon the later to occur of: (a) the date when [***] from the date of First Commercial Sale of the Licensed Treatment (the "Royalty Term").

6.4.3 Biosimilar Treatment. Upon entry of one or more Biosimilar Treatments in a country in the Territory, and where the total number of patients in such country receiving Biosimilar Treatments as their initial treatment reaches, in [***], a market share of [***] or greater of the total number of patients in such country receiving as their initial treatment, either Licensed Treatment or a Biosimilar Treatment (the "Biosimilar Market Trigger Event"), the Net Sales of Licensed Treatments in such country shall be reduced [***] before including same into total Net Sales in all countries in the Territory for the purpose of calculating the applicable royalty rates set forth in this Section 6.4. It is expressly understood and agreed, however, that (a) no such deduction to Net Sales shall apply to a Licensed Treatment (or its associated Licensed Treatment Monitoring Sales) to the extent the Licensed Treatment Administration Sale of such Licensed Treatment in such country occurred [***], and (b) such reduction shall cease in the event the foregoing [***] or greater market share condition is no longer satisfied in such country. All such determinations of patients shall be based upon a mutually acceptable calculation method using market share data provided by a reputable and mutually agreed upon provider, such as IMS Health, or similar data provider in countries where IMS Health is not operating.

6.4.4 Royalty Stacking. If Bayer reasonably determines in good faith that it is necessary to obtain either (i) a license from one or more Third Parties to make, have made, use, sell, offer to sell and/or import Licensed GT Products in the Field in one or more countries in the Territory, which such license is for a patent reasonably believed by Bayer to dominate one or more claims of Licensed Patents in existence as of the Original Effective Date and covering the Licensed GT Product, or (ii) a license under one or more process patents to make or have made the Licensed GT Product, and where, but for such license, Bayer would not be lawfully able to manufacture the Licensed GT Product, then in either or both cases, the amount of Bayer's royalty payments under Section 6.4 with respect to Net Sales for such Licensed GT Product for a given period shall be reduced by [***] of the amount of the payments paid under such other license(s) for that same period; provided that such Third Party payments are attributable to sales made by Bayer or its Affiliates or Sublicensees that are used in the calculation of Net Sales on which Bayer's royalty payment obligation to Dimension is based. Notwithstanding the foregoing, the adjustment of royalties under this Section 6.4.4 will in no event reduce the royalty rate to less than [***] of the applicable rate set forth in Section 6.4.1.

6.4.5 ReGenX Obligations. [***] shall be responsible for any and all payments owed to ReGenX pursuant to the ReGenX Agreement.

6.5 Reports and Records.

6.5.1 Bayer must deliver to Dimension within [***] after the end of each [***] after the First Commercial Sale of a Licensed Treatment a report setting forth the calculation of the royalties due to Dimension for such [***], including:

(a) Number of Licensed Treatments included within Net Sales, listed by country;

(b) Licensed Treatment Sales and Net Sales of Licensed Treatments listed by country;

(c) Royalties owed to Dimension, listed by category.

6.5.2 Upon receipt of an invoice, Bayer shall pay the royalties due under Section 6.4. If invoices are received by Bayer at the below address by [***], then payments shall be made by the [***] following the month in which the invoice was received. If invoices are received by Bayer at the below address after [***], then payments shall be made by the [***].

6.5.3 Bayer shall maintain and require its Affiliates and all Sublicensees to maintain, complete and accurate books and records that enable the royalties, fees, and payments payable under this Agreement to be verified. The records must be maintained for (a) [***] with respect to Bayer and its Sublicensees, and (b) [***] with respect to Bayer's Affiliates, in each case after the submission of each report under Article 6. No more frequently than once during each calendar year during the term of this Agreement and the [***] period thereafter, Bayer will permit Dimension's (or as applicable, ReGenX's or its licensors under the Existing Licenses) auditors from any auditing firm to which Bayer has no reasonable objection, and with at least [***] days advance notice at any time during normal business hours, accompanied at all times, to inspect, audit and copy reasonable amounts of relevant accounts and records of Bayer and its Affiliates and reports submitted to Bayer and its Affiliates from Sublicensees, for the sole purpose of verifying the accuracy of the calculation of payments to Dimension pursuant to this Section 6.5. The accounts, records and reports related to any particular period of time may only be audited one time under this Section 6.5. Dimension will cause its auditors not to provide Dimension with any copies of such accounts, records or reports and not to disclose to Dimension any information other than information relating solely to the accuracy of the accounting and payments made by Bayer pursuant to this Section. Dimension will cause its auditors to promptly provide a copy of their report to Bayer. If such audit determines that payments are due to Dimension, Bayer will, following receipt of an invoice, pay to Dimension any such additional amounts within [***] after the date on which such auditor's written report is delivered to Bayer and Dimension, unless such audit report is disputed by Bayer, in which case the dispute will be resolved in accordance with Section 13.6. If such audit determines that Bayer has overpaid any amounts to Dimension, Dimension will refund any such overpaid amounts to Bayer within [***] after the date on which such auditor's written report is delivered to Bayer and Dimension. Any such inspection of records will be at Dimension's expense unless such audit discloses a deficiency in the payments made by Bayer (whether for itself or on behalf of its Affiliates) of more than [***] of the aggregate amount payable for the relevant period, in which case Bayer will bear the cost of such audit. Notwithstanding anything to the contrary in and without limiting the foregoing, Bayer acknowledges and agrees that it may also be subject to the separate access or audit rights of ReGenX's licensors in accordance with the terms of the Existing Licenses, and if such a licensor exercises such access or audit rights, the provisions of Section 3.5.4 of the ReGenX Agreement will govern, unless such licensor otherwise consents to applying the provisions of this Section 6.5.3. Dimension acknowledges the disruption and effort required to provide information to be disclosed during an audit, and Dimension shall endeavor to avoid

multiple audits covering the same audit period. Without prejudice to the foregoing, Dimension shall not conduct an audit of any period for which ReGenX or any of the licensors under the Existing Licenses have already conducted an audit or have given notice that they intend to conduct such an audit. In addition, Dimension shall enforce any rights it has under the ReGenX Agreement to limit the scope of any audit that might be demanded pursuant to the ReGenX Agreement.

6.6 Payment, Currency, Interest.

6.6.1 Payment Address. All invoices shall be sent to the following address:

Bayer HealthCare
Pharma West Coast
PO Box 416
Pittsburgh PA 15230
USA

6.6.2 Payments made by Wire Transfer. All payments made to Dimension under the Agreement shall be made by wire transfer to the following bank account, or such other bank account as notified by Dimension to Bayer from time to time:

Wire Transfer Instructions
[***]
[***]
[***]
[***]
[***]

6.6.3 All dollar amounts referred to in this Agreement are expressed in United States dollars. All payments to Dimension under this Agreement must be made in United States dollars.

6.6.4 Net Sales made in currencies other than USD will be converted into USD using the average exchange rate for the applicable [***] as for Bayer's internal accounting and reporting process consistently applied, which in any event shall comply with IFRS.

6.6.5 Any payments due under the Agreement shall be due on such date as specified in the Agreement. Any failure by Bayer to make a payment by the date when due shall obligate Bayer to pay interest on the due payment to Dimension. The interest period shall commence on the due date (inclusive) and end on the payment date (exclusive). Interest shall be calculated based on the actual number of days in the interest period divided by 360. The interest rate shall be equal to [***], plus a premium of one percentage point, or shall be equal to an interest rate according to local legal provisions, whatever is lower.

6.6.6 All payments by Bayer to Dimension for funding of the Research Program are as set forth in and will be in accordance with Section 2.5.

6.7 Withholding Tax. The Parties agree to cooperate with one another and use reasonable efforts to reduce or eliminate tax withholding or similar obligations in respect of

royalties, milestone payments, and other payments made by Bayer to Dimension under this Agreement. Any Party required to make a payment under this Agreement shall be entitled to deduct and withhold from the amount payable the tax for which the paying Party is liable under any provision of applicable tax law. No deduction shall be made or a reduced amount shall be deducted if the paying Party is timely furnished by payee with all documents required for the application of a zero or reduced rate according to the respective Double Taxation Treaty. Any withheld tax shall be treated as having been paid by paying Party to payee for all purposes of this Agreement, provided that each Party shall provide the other with reasonable assistance to enable the recovery, as permitted by applicable Laws, of such withholding taxes, such recovery to be for the benefit of the Party bearing such withholding tax. Paying Party shall timely forward the tax receipts certifying the payments of withholding tax on behalf of payee. Any assignment of this Agreement by paying Party which causes a higher withholding tax rate than would be applicable without the assignment shall be borne by paying Party. If paying Party failed to deduct withholding tax but is still required by applicable tax law to pay withholding tax on account of payee to the tax authorities, payee shall assist paying Party with regard to all procedures required in order to obtain reimbursement by tax authorities or, in case tax authorities will not reimburse withholding tax to paying Party, payee will immediately refund the tax amount.

6.8 Value Added Tax. All agreed consideration is exclusive of Value Added Tax ("VAT"). VAT applies and shall be invoiced additionally according to the applicable VAT law and shall be paid to Dimension, if payable by Dimension to the respective tax authority and after receipt of a correct invoice in accordance with the applicable VAT law.

ARTICLE 7: DILIGENCE

7.1 Diligence Obligations. Bayer will use Commercially Reasonable Efforts to complete the POC Trial and to develop, Commercialize, market, promote, and sell at least one Licensed GT Product or Licensed Treatment in the Field in the US and the Major Market Countries.

7.2 Development Plans. The Parties acknowledge that pursuant to the ReGenX Agreement, Dimension is required to provide ReGenX with a development plan and budget covering the [***] of development activities with respect to the Licensed GT Product and Licensed Treatment, and to provide [***] updates to such development plan and budget. Bayer agrees to cooperate with Dimension in the provision of information in meeting Dimension's obligation under the ReGenX Agreement, and such cooperation may include sharing a copy of the Research Plan (or portions thereof) with ReGenX, answering follow up questions ReGenX may have, or providing certain information regarding the clinical development and regulatory activities by Bayer and its Affiliates and Sublicensees with respect to the POC Trial Material or Licensed GT Product, as applicable.

7.3 Development Reporting. Within [***] of [***] during the term of this Agreement, Bayer shall provide Dimension with written progress reports through the JSC and JPT, setting forth in reasonable detail the progress of the conduct of the POC Trial, to the extent relating to obligations that have been allocated to it, and the development, evaluation, testing, and commercialization of each Licensed GT Product and Licensed Treatment. Bayer will also notify Dimension within [***] of the First Commercial Sale by Bayer, its Affiliates, or any

Sublicensees of each Licensed Treatment. Such a report ("Development Progress Report"), setting forth the current stage of development of Licensed GT Products, shall include:

7.3.1 Date of Development Progress Report and time covered by such report;

7.3.2 Major activities and accomplishments completed by Bayer, its Affiliates, and any Sublicensees relating directly to the Licensed GT Product since the last Development Progress Report;

7.3.3 Significant research and development projects relating directly to the Licensed GT Product currently being performed by Bayer, its Affiliates, and any Sublicensees and projected dates of completion;

7.3.4 Development activities anticipated for the next [***];

7.3.5 Projected total development remaining before product launch of each Licensed Treatment; and

7.3.6 Summary of significant development efforts using the Sublicensed Technology being performed by Third Parties, including the nature of the relationship between Bayer and such Third Parties.

7.4 Confidential Information. The Parties agree that Development Progress Reports shall be deemed Bayer's Confidential Information; provided that Dimension may share a copy of such reports with ReGenX and with ReGenX's licensors under the Existing Licenses, subject to obligations of confidentiality.

7.5 Improvements. Simultaneously with the Development Progress Report, Bayer shall deliver a detailed description of any Licensed Back Improvements, if not previously provided.

ARTICLE 8: CONFIDENTIALITY

8.1 Treatment of Confidential Information. Each Party, as a receiving party (a "Receiving Party"), agrees that it will (a) treat Confidential Information of the other Party (the "Disclosing Party") as strictly confidential; (b) not disclose such Confidential Information to Third Parties without the prior written consent of the Disclosing Party, except as may be permitted in this Agreement; provided that any disclosure permitted hereunder be under confidentiality agreements with provisions at least as stringent as those contained in this Agreement; and (c) not use such Confidential Information for purposes other than those authorized expressly in this Agreement. The Receiving Party agrees to ensure that its employees who have access to Confidential Information of the other Party are obligated in writing to abide by confidentiality obligations at least as stringent as those contained under this Agreement. Dimension shall also maintain Licensed Know-How as confidential to the extent that it relates solely to the Field, subject to the provisions of this Article 8.

8.2 Public Announcements.

8.2.1 The Parties agree they will each issue a press release in a form as outlined in Exhibit F and at such time as is agreed upon by the Parties. Except as provided in Section 8.2.3, Section 8.3 and Section 8.4, any other press releases by either Party with respect to the other Party or any other public disclosures concerning the existence of or terms of this Agreement shall be subject to review and approval by the other Party.

8.2.2 After release of such agreed upon press release, if either Party desires to make a public announcement concerning the material terms of this Agreement or any activities hereunder, such Party shall give reasonable prior advance notice of the proposed text of such announcement to the other Party for its prior review and approval (except as otherwise provided herein), which approval shall not be unreasonably withheld or delayed, except that in the case of a press release or governmental filing determined by such Party, based on advice of counsel, to be required by law, the disclosing Party shall provide the other Party with such advance notice as it reasonably can and shall not be required to obtain approval therefor. Neither Party shall be required to seek the permission of the other Party to repeat any information that has already been publicly disclosed by such Party, or by the other Party, in accordance with this Section 8.2, provided such information remains accurate as of such time.

8.2.3 The Parties acknowledge that either or both Parties may be obligated to file under applicable Laws a copy of this Agreement with the U.S. Securities and Exchange Commission or other governmental authorities both in the US and elsewhere. Each Party shall be entitled to make such a required filing, provided that it requests confidential treatment of the confidential commercial terms and sensitive technical terms hereof and thereof to the extent such confidential treatment is reasonably available to such Party. In the event of any such filing, each Party will provide the other Party with a copy of this Agreement marked to show provisions for which such Party intends to seek confidential treatment and shall reasonably consider and incorporate the other Party's reasonable comments thereon to the extent consistent with the legal requirements, with respect to the filing Party, governing disclosure of material agreements and material information that must be publicly filed.

8.3 Authorized Disclosure. Notwithstanding the provisions of Section 8.1 or 8.2, either Party may disclose Confidential Information of the other Party, or make such a disclosure of the existence of and/or terms of this Agreement:

8.3.1 to any Affiliates, legal advisors, accountants, and, in each case whether actual or bona fide potential, to collaboration partners (such as CMOs, CROs and other vendors providing services relating to the subject matter of the Agreement), licensees, acquirers, investors, lenders, and other potential financing sources; provided that, in each case, such recipient of Confidential Information is obligated to keep such information confidential on terms no less stringent than those set forth in this Agreement.

8.3.2 if such disclosure is reasonably necessary (i) for filing or prosecuting Patent Rights as contemplated by this Agreement; (ii) to comply with the requirements of regulatory authorities with respect to obtaining and maintaining Regulatory Approval of a Licensed GT Product or Licensed Treatment; or (iii) for prosecuting or defending litigation;

8.3.3 such disclosure is reasonably necessary or desirable to comply with applicable Laws, including regulations promulgated by applicable security exchanges, court order, administrative subpoena or order;

8.3.4 in connection with Bayer's development, manufacture or Commercialization of the Licensed GT Products or Licensed Treatment in the Field in the Territory, including, without limitation, to existing or potential distributors, service providers, Sublicensees, Affiliates, or collaboration partners, contractors or investigators, under substantially the same confidentiality obligations as are set forth herein, except that the confidentiality obligations shall have a term of at least [***]; or

8.3.5 such disclosure is to ReGenX and its licensors solely as required under the terms of, and subject to, the ReGenX Agreement, and under the condition that ReGenX does not disclose Confidential Information to others (except as may be required under the Existing Licenses).

8.4 Compelled Disclosure. In the event that the Receiving Party receives service of legal process that purports to compel disclosure of the Disclosing Party's Confidential Information or becomes obligated by Law to disclose the Confidential Information of the Disclosing Party or the existence of or terms of this Agreement to any governmental authority, the Receiving Party shall promptly notify the Disclosing Party, so that the Disclosing Party may seek an appropriate protective order or other remedy with respect to narrowing the scope of such requirement and/or waive compliance by the Receiving Party with the provisions of this Agreement. The Receiving Party will provide the Disclosing Party with reasonable assistance in obtaining such protective order or other remedy. If, in the absence of such protective order or other remedy, the Receiving Party is nonetheless required by Law to disclose the existence of or terms of this Agreement or other Confidential Information of the Disclosing Party, the Receiving Party may disclose such Confidential Information without liability hereunder; provided that the Receiving Party shall furnish only such portion of the Confidential Information that is legally required to be disclosed and only to the extent required by Law.

8.5 Term of Confidentiality. The obligations of this Article 8 shall continue for a period of [***] following the expiration or termination of this Agreement.

ARTICLE 9: TERM AND TERMINATION

9.1 Term of Agreement. This Agreement, unless sooner terminated as provided in this Agreement, expires upon the expiration of the Royalty Term. Upon expiration of this Agreement (but not early termination), (a) Bayer's license to Licensed Know-How under Section 5.1 will become non-exclusive, perpetual, irrevocable, [***] with respect to the Dimension Know-How and Sublicensed Know-How, provided that with respect to Sublicensed Know-How such license will remain limited to the Field and subject to the Retained Rights, and (b) Bayer's license to Dimension Manufacturing Patents under Section 5.1(b) will become perpetual.

9.2 Bayer's Right to Terminate for Convenience. At any time Bayer may, upon [***] prior written notice to Dimension, terminate this Agreement for any reason. In exercising such termination right, Bayer may terminate the Agreement in its entirety or, if desired, Bayer may

specify in the written notice that this Agreement is terminating only with respect to one or more country within the Territory; provided, however, that, should Bayer terminate with respect to both the U.S. and all Major Market Countries, this Agreement will terminate in its entirely unless otherwise agreed by the Parties.

9.3 Bayer's Right to Terminate for Safety. In the event that, during or following the POC Trial, Bayer makes a good faith determination in accordance with its standard practices and procedures for such determinations that there is a material safety issue with respect to the GT Product that comprises the POC Trial Material or Licensed GT Product in the Field in the Territory Bayer may terminate this Agreement upon [***] notice.

9.4 Bayer's Right to Terminate for Failure to achieve Demonstration of Clinical POC. If the initial Licensed GT Product or the Backup Product fails to achieve Demonstration of Clinical POC Bayer may, within [***] of being notified of such failure, upon [***] notice, terminate this Agreement.

9.5 Termination for Breach. Dimension may terminate this Agreement if Bayer is late in paying to Dimension any milestones or royalties, fees or any other monies due under this Agreement, and Bayer does not pay Dimension in full within [***] upon written demand from Dimension, which termination shall be effective immediately upon the expiration of such [***] cure period, provided that no demand will be issued prior to expiration of the due date for payment, and provided further that Bayer is not disputing on a bona fide basis that a payment is due. Either Party may terminate this Agreement, if the other Party materially breaches (other than nonpayment) this Agreement and does not cure such material breach within [***] after written notice of the breach, which termination shall be effective immediately upon the expiration of such [***] cure period. Notwithstanding the foregoing, if the default is not reasonably capable of being cured within the [***] cure period by the defaulting Party and such defaulting Party is making a good faith effort to cure such default, the cure period shall be extended by no more than [***]. Bayer acknowledges and understands that: (a) in the event the nature of a breach by Bayer causes Dimension (as a sublicensor hereunder) to be in breach of the ReGenX Agreement, the applicable cure periods as set forth in the ReGenX Agreement are shorter than those set forth in this Section 9.5; and further, (b) with respect to such breach by Bayer described in (a), Dimension shall not be responsible for any termination by ReGenX through exercise of ReGenX's termination right under the ReGenX Agreement, where such termination occurs prior to the [***] cure period given to Bayer above. For the avoidance of doubt, Bayer shall not be liable or otherwise responsible to Dimension for any loss, costs, expenses, damages or liability of any kind arising from a breach or termination of the ReGenX Agreement attributable to Bayer's exercise of its rights under this Agreement. The right of either Party to terminate this Agreement as herein above provided shall not be affected in any way by its waiver of, or failure to take action with respect to, any previous default.

9.6 Patent Challenge. Dimension may terminate this Agreement if Bayer or any of its Affiliates institutes a Patent Challenge. Such termination will be effective [***] days after written notice from Dimension to Bayer unless within such [***] days Bayer or its Affiliates causes such Patent Challenge to terminate. "Patent Challenge" means any [***].

9.7 Termination for Insolvency.

9.7.1 Dimension may terminate this Agreement, effective immediately upon written notice to Bayer, if Bayer or any of its Controlling Affiliates experiences any Trigger Event.

9.7.2 Bayer shall include in each sublicense agreement entered into with a Sublicensee a right of Bayer to terminate such sublicense agreement if such Sublicensee experiences any event corresponding to a Trigger Event; and Bayer shall terminate the sublicense agreement, effective immediately upon written notice to the Sublicensee, if the Sublicensee experiences any such event.

9.7.3 For purposes of this Section 9.7, "Trigger Event" means any of the following (provided they are not for purposes of reorganization): (a) if Bayer (i) becomes insolvent, becomes bankrupt, or generally fails to pay its debts as such debts become due, (ii) is adjudicated insolvent or bankrupt, (iii) admits in writing its inability to pay its debts, (iv) suffers the appointment of a custodian, receiver, or trustee for it or its property and, if appointed without its consent, is not discharged within [***], (v) makes an assignment for the benefit of creditors, or (vi) suffers proceedings being instituted against it under any law related to bankruptcy, insolvency, liquidation, or the reorganization, readjustment, or release of debtors and, if contested by it, not dismissed or stayed within [***]; or (b) the calling by Bayer of a meeting of its creditors with a view to arranging a composition or adjustment of its debts. Bayer acknowledges and understands that: (1) the timing periods in (iv) and (vi) above differ from those set forth in the definition of "Trigger Event" in Section 6.4.3 of the ReGenX Agreement, which are [***] and [***], respectively, and (2) in the event such difference causes Dimension (as a sublicensor hereunder) to be in breach of the ReGenX Agreement, Dimension shall not be responsible for any termination by ReGenX through exercise of ReGenX's termination right under the ReGenX Agreement, where the termination is due to such difference. Bayer shall not be liable or otherwise responsible to Dimension for any loss, costs, expenses, damages or liability of any kind arising from a breach or termination of the ReGenX Agreement due to such difference or otherwise attributable to Bayer's exercise of its rights under this Agreement.

9.8 Applicability of Section 365(n) of the Bankruptcy Code. In the event either Party becomes a debtor under Title 11 of the U.S. Code, this Agreement shall be deemed to be, for purposes of Section 365(n) of Title 11, a license to "Intellectual Property" as defined therein and the other Party and its Affiliates, and each of their successors and assigns as licensees shall have the rights and elections as specified in Section 365(n) of Title 11 of the U.S. Code. Without limiting the foregoing, upon termination of this Agreement by a trustee or executor of either Party which has rejected this Agreement pursuant to any non-contractual rights afforded to it by applicable bankruptcy law and/or a U.S. or foreign bankruptcy court or other tribunal of competent jurisdiction, all rights and licenses herein granted to the other Party shall nonetheless continue in full force and effect in accordance with the terms of this Agreement.

9.9 Effects of Termination. The effect of termination by Bayer pursuant to Sections 9.2, 9.3, or 9.4 and by either Party, as applicable, under Sections 9.5 or 9.7, or by Dimension pursuant to Section 9.6 shall be as follows:

9.9.1 The licenses and sublicenses granted by Dimension hereunder shall terminate, and Bayer, its Affiliates, and (unless the sublicense agreement is assigned pursuant to

Section 9.9.2) all Sublicensees shall cease to make, have made, use, import, sell, and offer for sale all Licensed GT Products and shall cease to otherwise practice the Licensed Technology and Dimension POC Technology; provided that Bayer, its Affiliates, and Sublicensees, shall have the right to continue to sell their existing inventories of Licensed GT Products for a period not to exceed [***] after the effective date of such termination, and provided also that Bayer, its Affiliates and Sublicensees shall have the right to continue to supply Licensed GT Products or support any Licensed Treatment to the extent required by any Regulatory Authority, but in each case subject to any payment obligations to Dimension under Article 6;

9.9.2 Bayer shall have the right to assign to Dimension any or all sublicenses granted to Third Parties to the extent of the rights licensed to Bayer hereunder and sublicensed to the Sublicensee; provided that (i) prior to such assignment, Bayer shall advise Dimension whether such Sublicensee is then in full compliance with all terms and conditions of its sublicense and continues to perform thereunder, and, if such Sublicensee is not in full compliance or is not continuing to perform, Dimension may elect not to have such sublicense assigned; and (ii) such assignment shall be subject to Dimension not being liable to such Sublicensee with respect to any obligations of Bayer to the Sublicensee that are not consistent with, or not required by, Dimension's obligations to Bayer under this Agreement; and all sublicenses not requested to be assigned to Dimension shall terminate;

9.9.3 If termination is by Bayer pursuant to Section 9.2, 9.3 or 9.4, or by Dimension pursuant to Section 9.5, 9.6, or 9.7:

(a) if, at the time of such termination, there are any ongoing clinical trials with respect to the POC Trial Material or Licensed GT Products in the Field, the Parties shall, at Dimension's option, negotiate in good faith and adopt a plan to wind-down such trial activities in an orderly fashion at Bayer's expense or, at Dimension's election, promptly transition such development activities to Dimension or its designee, with due regard for patient safety and the rights of any subjects that are participants in any such clinical trials and take any actions Dimension deems reasonably necessary or appropriate to avoid any human health or safety problems and in compliance with all applicable Laws; and

(b) Bayer shall grant, and hereby grants (effective only upon any such termination of this Agreement), to Dimension a non-exclusive, perpetual, irrevocable, worldwide, [***], transferable, sublicensable license to any Licensed Back Improvements, for use by Dimension and ReGenX for the research, development, and commercialization of products in any therapeutic indication.

9.9.4 If termination is by Bayer pursuant to Section 9.2:

(a) Bayer shall grant, and hereby grants (effective only upon any such termination of this Agreement), to Dimension an exclusive (even as to Bayer), worldwide, [***], transferable, perpetual, irrevocable license, with the right to grant sublicenses, under the Bayer Technology to make, have made, use, import, sell, and offer for sale the POC Trial Material, Licensed GT Products or any Licensed Treatments as they were being developed or Commercialized at the time of termination, solely in the

Field. For this purpose, the "Bayer Technology" means Bayer's patents, Know-How, and other intellectual property that are improvements or modifications to or that are based on or derived in whole or in part from or that otherwise relate to any Licensed Technology or Dimension POC Technology to the extent such patents, Know-How (including all data and regulatory submissions), or other intellectual property pertains to the POC Trial Material, Licensed GT Products or Licensed Treatments that were being developed or Commercialized by Bayer at the time of termination. To effectuate such license, upon any such termination of this Agreement, Bayer will promptly disclose to Dimension all Bayer Technology not already known to Dimension;

(b) Bayer will transfer to Dimension ownership of any Regulatory Approvals then in Bayer's, its Affiliates', or any Sublicensee's (to the extent a sublicense is terminated and not assigned) name related to the POC Trial Material or Licensed GT Products as then being developed or Commercialized containing any expression construct provided by Dimension to Bayer as part of the Dimension POC Technology or Licensed Technology and notify the appropriate regulatory authorities and take any other action reasonably necessary to effect such transfer of ownership; and

(c) At Dimension's request Bayer shall transfer any biological materials or compounds that Bayer has manufactured or had manufactured relating to the POC Trial Material, Licensed GT Product or Licensed Treatment and that is in Bayer's possession as at the date of termination. Dimension shall pay for such materials and compounds at cost, without any markup.

9.9.5 If termination occurs prior to completion of the POC Trial for whatever reason, Bayer shall transfer to Dimension or its designee the First IND together with any of its foreign counterparts, including any supplements or amendments that may exist as at the effective date of termination.

9.9.6 The Parties acknowledge and agree that, if the GSK Agreement is terminated as described in Section 6.5 of the GSK Agreement, then, as provided in Section 6.5.2 thereof, ReGenX will assign the ReGenX Agreement to the licensor of the GSK Agreement to the extent the ReGenX Agreement is related solely to the rights and products licensed to ReGenX under the GSK Agreement.

9.9.7 Each Receiving Party shall, at the other Party's request, return all Confidential Information and any remaining Materials of the Disclosing Party. Notwithstanding the foregoing, one copy of such Confidential Information may be kept by either Party for a record of that Party's obligations.

If termination is only with respect to a particular country or region within the Territory, but not all countries, then the provisions of this Section 9.9 shall only apply with respect to the terminated country(ies), and this Agreement shall continue with respect to the non-terminated countries.

9.10 Survival. Bayer's obligation to pay all monies due and owed to Dimension under this Agreement which have matured as of the effective date of termination or expiration shall

survive the termination or expiration of this Agreement. In addition, the provisions of Sections 5.11.2 (Exclusivity: Bayer), 9.1 (Term of Agreement), 9.8 (Applicability of Section 365(n) of the Bankruptcy Code), 9.9 (Effects of Termination), 9.10 (Survival), 10.1 (Ownership of Inventions), 11.4 (Disclaimer of Warranties, Damages), and 11.5 (Indemnification), and Articles 1 (Definitions), 6 (Consideration) (but only in respect of payments that have accrued and become payable prior to the effective date of termination), 8 (Confidentiality), 12 (Use of Name) and 13 (Additional Provisions) shall survive such termination or expiration of this Agreement in accordance with their respective terms.

ARTICLE 10: PATENT MAINTENANCE; PATENT INFRINGEMENT

10.1 Ownership of Inventions. Each Party shall own all Know-How generated solely by it and its Affiliates and their respective employees, agents and independent contractors in the course of conducting such Party's activities under this Agreement ("Sole Inventions") and any Patent Rights arising therefrom (the "Bayer Patents" in the case of Bayer's Sole Inventions). All Know-How generated jointly by employees, Affiliates, agents, or independent contractors of each Party in the course of performing activities under this Agreement (collectively, "Joint Inventions"), and all Patent Rights contained within such Joint Inventions (collectively, "Joint Patents"), shall be owned jointly by the Parties in accordance with joint ownership interests of co-inventors under U.S. patent laws (that is, each Party shall have full rights to license, assign and exploit such Joint Inventions (and any patents arising therefrom) anywhere in the world, without any requirement of gaining the consent of, or accounting to, the other Party), subject to the covenants and licenses granted herein and subject to any other intellectual property held by such other Party. For purposes of determining whether Inventorship shall be a Sole Invention or a Joint Invention under this Agreement, inventorship shall be determined in accordance with U.S. patent laws.

10.2 Disclosure of Inventions. Dimension shall promptly disclose to Bayer all Sole Inventions, and each Party shall promptly disclose to the other Party any Joint Inventions, including any invention disclosures or similar documents submitted to it by its employees, agents or independent contractors describing such inventions, and all other information relating to such inventions to the extent necessary or useful for the preparation, filing and maintenance of any Patent Rights with respect to such inventions.

10.3 Prosecution of Dimension Patents. As between Dimension and Bayer, the Parties agree as follows:

10.3.1 Dimension shall have the sole right to Prosecute patent applications and issued patents within Dimension Patents in Dimension's sole discretion and at its own expense. Dimension shall provide Bayer with a reasonable opportunity to review and provide comments in connection with the Prosecution of the Dimension Patents; and Dimension shall keep Bayer reasonably informed as to all material developments with respect to such Dimension Patents and shall supply to Bayer copies of material communications received and filed in connection with the Prosecution of such Dimension Patents.

10.3.2 Dimension agrees to Prosecute any patent applications or issued patents within the Dimension Patents in good faith. If Dimension decides not to file, to abandon

or not to maintain any of such Dimension Patents, in each case where a claim may cover a Licensed GT Product or GT Product, then Dimension shall provide Bayer with [***] prior written notice of such decision (or such other longer period of time reasonably necessary to allow Bayer to assume such responsibilities, at the sole discretion of Dimension). In such event, Bayer shall have the right, at its option, to the extent Dimension is permitted by obligations owed to Third Parties, to have assigned to it the said Dimension Patents. If assignment is not possible, Bayer shall have a non-exclusive, perpetual, irrevocable, royalty-free license with respect to those Dimension Patents. In either case (assignment or non-exclusive license) the Patent Rights will cease to be Dimension Patents.

10.4 Prosecution of Joint Patents. As between Dimension and Bayer, the Parties agree as follows:

10.4.1 Dimension shall have the sole right to Prosecute patent applications and issued patents within Joint Patents in Dimension's discretion and at its own expense. Dimension shall provide Bayer with a reasonable opportunity to review and provide comments in connection with the Prosecution of the Joint Patents; and Dimension shall keep Bayer reasonably informed as to all material developments with respect to such Joint Patents and shall supply to Bayer copies of material communications received and filed in connection with the Prosecution of such Joint Patents.

10.4.2 Dimension agrees to Prosecute any patent applications or issued patents within the Joint Patents in good faith. If Dimension decides not to file, to abandon or not to maintain any of such Joint Patents, then Dimension shall provide Bayer with [***] prior written notice of such decision (or such other longer period of time reasonably necessary to allow Bayer to assume such responsibilities, at the sole discretion of Dimension). In such event, Bayer shall have the right, at its option, to have assigned to it Dimension's interest in such Joint Patents, and such Patent Rights shall cease to be Dimension Patents.

10.5 Prosecution of Bayer Patents. As between Dimension and Bayer, the Parties agree as follows:

10.5.1 Bayer shall have the sole right to Prosecute patent applications and issued patents within Bayer Patents in Bayer's sole discretion and at its own expense. Bayer shall provide Dimension with a reasonable opportunity to review and provide comments in connection with the Prosecution of the Bayer Patents; and Bayer shall keep Dimension reasonably informed as to all material developments with respect to such Bayer Patents and shall supply to Dimension copies of material communications received and filed in connection with the Prosecution of such Bayer Patents.

10.5.2 Bayer agrees to Prosecute any patent applications or issued patents within the Bayer Patents in good faith. If Bayer decides not to file, to abandon or not to maintain any of such Bayer Patents that claim only a Licensed GT Product or GT Product and no other product or component thereof, then Bayer shall provide Bayer with [***] prior written notice of such decision (or such other longer period of time reasonably necessary to allow Dimension to assume such responsibilities, at the sole discretion of Bayer). In such event, Dimension shall have the right, at its option, to control the filing, prosecution and/or maintenance of any such

Bayer Patents, at its own expense, and the Parties shall have the rights with respect to such Bayer Patents as set forth in Section 10.5.1 (with the Parties' roles reversed).

10.6 Prosecution of Sublicensed Patents. Bayer acknowledges and agrees that, in accordance with the terms of the ReGenX Agreement:

10.6.1 ReGenX retains the sole right to Prosecute patent applications and issued patents within the Sublicensed Patents, in ReGenX's sole discretion. Subject to Section 10.6.3, and subject to ReGenX providing Dimension with a reasonable opportunity to review and provide comments in connection with the Prosecution of the Sublicensed Patents, Dimension shall provide Bayer with same, to the extent such Sublicensed Patents cover or claim the Licensed GT Products in the Field; and Dimension shall keep Bayer reasonably informed as to all material developments with respect to such Sublicensed Patents and shall supply to Bayer copies of material communications received from ReGenX and filed in connection with the Prosecution of such Sublicensed Patents.

10.6.2 Bayer acknowledges that [***] has no obligation to undertake any inter-party proceedings, such as oppositions or interferences, or to undertake any re-examination or re-issue proceedings, in either case, with respect to the Sublicensed Patents.

10.6.3 Bayer acknowledges that the University of Pennsylvania controls Prosecution of the Sublicensed Patents under the Penn Agreement, with ReGenX having certain rights to review.

10.7 Product Infringement Actions Against Third Parties.

10.7.1 Notification. If either Party becomes aware of any existing or threatened infringement of any Dimension Patent, Bayer Patent or Sublicensed Patent by the manufacture, use or sale of a gene therapy product for use in the Field (a "Product Infringement"), it shall promptly notify the other Party in writing to that effect, and the Parties will consult with each other regarding any actions to be taken with respect to such Product Infringement.

10.7.2 Dimension Patents (including Joint Patents). As between Dimension and Bayer, the Parties agree as follows:

10.7.2.1 [***] shall have the first right, but not the obligation, to prosecute any Product Infringement of those Dimension Patents (including Joint Patents) in each case that claim [***] (the "[***] Patents") at its own expense. In any action to enforce any of such [***] Patents, [***], at the request and [***], shall [***], including in the event that, [***].

10.7.2.2 If [***] elects not to pursue any infringement of a [***] Patent, [***] shall have the second right, but not obligation, to prosecute such Product Infringement of such [***] Patents, at [***]. In any such action to enforce any of the [***] Patents, [***], at the request and [***], shall [***]. In prosecuting any such Product Infringement, [***].

10.7.2.3 [***] shall have the right, but not the obligation, to prosecute any infringement of those Dimension Patents (including Joint Patents) that are not [***] Patents (the "[***]Patents") in its sole discretion. If [***] elects not to pursue any infringement of a [***] Patent in a country in the Territory, provided that such [***] Patent is [***], [***] shall have the second right, but not the obligation, to prosecute a Product Infringement of such [***] Patent, at [***] expense, in such country. If any Third Parties also have licenses under such [***] Patents, [***] shall take account of such Third Party rights in exercising its rights hereunder, and shall take [***] In any such action by [***] to enforce any of the [***] Patents, [***], at the request [***], shall [***], including in the event that, [***]. In prosecuting any such Product Infringement, [***].

10.7.2.4 Any recovery of damages by Bayer or Dimension for any Product Infringement pursuant to this Section 10.7.2 shall be applied, as between Dimension and Bayer, first to reimburse each such Party for costs and expenses (including reasonable attorneys' fees and costs) incurred by such Party in connection with such suit, second, compensatory damages will be [***], and the balance remaining, if any, from any such recovery shall be [***].

10.7.3 Enforcement of Joint Patents in [***]. As between Dimension and Bayer, the Parties agree as follows:

10.7.3.1 [***] shall have the first right, but not obligation, to prosecute any infringement of Joint Patents that is [***], at [***] expense. In any action to enforce any of such Joint Patents, [***], at the request [***], shall [***], including in the event that, [***].

10.7.3.2 If [***] elects not to pursue any such infringement of a Joint Patent, then [***] shall have the second right, but not obligation, to prosecute such infringement of the Joint Patent, at [***]. In any such action to enforce any of the Joint Patents, [***], at the request [***], shall [***], including in the event that, [***].

10.7.3.3 Any recovery of damages by the Party undertaking enforcement or defense of a suit for infringement of a Joint Patent under this Section 10.7.3 shall be applied, as between Bayer and Bayer, first to reimburse each such Party for costs and expenses (including reasonable attorneys' fees and costs) incurred by such Party in connection with such suit, second, compensatory damages will be [***], and the balance remaining, if any, from any such recovery shall be [***].

10.7.4 Sublicensed Patents. Bayer acknowledges and agrees that, in accordance with the ReGenX Agreement:

10.7.4.1 Bayer understands and acknowledges that pursuant to the ReGenX Agreement, [***] has the first right, but not the obligation, to prosecute any infringement of Sublicensed Patents at [***]. In any action to enforce any of the Sublicensed Patents, [***], at the request [***], shall [***], including in the event that, [***].

10.7.4.2 If [***] elects not to pursue any infringement of a Sublicensed Patent and such Sublicensed Patent is being infringed by [***], then as between [***] and [***], [***] shall have the first right [***], but not obligation, to prosecute such [***]

with respect to such [***], at [***] expense. In any such action to enforce any of the Sublicensed Patents, [***], at the request [***], shall [***], including in the event that, [***]. In prosecuting any such [***].

10.7.4.3 Any recovery of damages by [***] for any infringement other than a [***] shall be retained [***]. Any recovery of damages by the Party undertaking enforcement or defense of a suit for [***] shall be applied, as between [***], first to reimburse each such Party for costs and expenses (including reasonable attorneys' fees and costs) incurred by such Party in connection with such suit, and the balance remaining, if any, from any such recovery shall be, [***].

10.7.4.4 Bayer acknowledges and agrees that [***] obligations under the ReGenX Agreement to enforce any Sublicensed Patents [***], and that [***] retain the [***] right to [***], all as set forth in the ReGenX Agreement and the Existing Licenses. Dimension will [***] under the ReGenX Agreement if reasonably requested by Bayer.

10.8 Defense of Infringement Claims.

10.8.1 In the event Bayer or Dimension becomes aware that Bayer's or any of its Affiliates' or any Sublicensees' practice of any invention claimed in the Sublicensed Patents or Dimension Patents is the subject of a claim of infringement of any patent owned by a Third Party, that Party shall promptly notify the other, but Bayer shall have exclusive right to take action to defend or abate any such claim brought against Bayer or any of its Affiliates or Sublicensees, and shall do so at its own expense and subject to Section 10.8.2.

10.8.2 Without Dimension's prior written permission, Bayer must not settle or compromise any such suit in a manner that imposes any material obligations or restrictions on ReGenX or any of its direct or indirect licensors under the Existing Licenses or grants any rights to the Sublicensed Patents or Dimension Patents other than rights that Bayer has the right to grant under this Agreement.

ARTICLE 11: WARRANTIES; INDEMNIFICATION

11.1 Mutual Representations and Warranties. Each Party hereby represents and warrants to the other Party as follows:

11.1.1 Corporate Existence. As of the Original Effective Date, it is a company or corporation duly organized, validly existing, and in good standing under the Laws of the jurisdiction in which it is incorporated.

11.1.2 Corporate Power, Authority and Binding Agreement. As of the Original Effective Date, (i) it has the corporate power and authority and the legal right to enter into this Agreement and perform its obligations hereunder; (ii) it has taken all necessary corporate action on its part required to authorize the execution and delivery of this Agreement and the performance of its obligations hereunder; and (iii) this Agreement has been duly executed and delivered on behalf of such Party, and constitutes a legal, valid, and binding obligation of such Party that is enforceable against it in accordance with its terms.

11.2 Additional Representations and Warranties of Dimension. Dimension represents and warrants as of the Original Effective Date and, as applicable, covenants to Bayer as follows:

11.2.1 Title; Control; Encumbrances. Dimension has not granted any Third Party any rights under any Licensed Patents in existence as of the Original Effective Date, and to Dimension's knowledge, all Licensed Know-How in existence as of the Original Effective Date is free and clear from any mortgages, pledges, liens, security interests, conditional and installment sale agreements, encumbrances, charges or claims of any kind (subject to the rights retained by ReGenX in the ReGenX Agreement). Dimension has the full and legal rights and authority to license to Bayer the Licensed Technology in the manner set forth in this Agreement;

11.2.2 Inventorship. To Dimension's knowledge, the inventorship of each Licensed Patent is properly identified on each such patent;

11.2.3 Good Standing. To Dimension's knowledge, all official fees, maintenance fees and annuities for the Licensed Patents have been paid and all administrative procedures with patent offices have been completed for the Licensed Patents such that the Licensed Patents are subsisting and in good standing;

11.2.4 Duty of Disclosure. Dimension has complied with and, to Dimension's knowledge ReGenX has complied with, the U.S. PTO duty of disclosure respecting the prosecution of all of Dimension Patents and, in the case of ReGenX, the Sublicensed Patents;

11.2.5 Notice of Infringement/Misappropriate. Dimension has not received any written notice from any Third Party asserting or alleging, nor does Dimension have any knowledge of any basis for any assertion or allegation, that any research, manufacture or development of GT Products by Dimension prior to the Original Effective Date infringed or misappropriated the intellectual property rights of such Third Party;

11.2.6 No Conflicts. Dimension has not entered, and shall not enter, into any agreement with any Third Party that is in conflict with the rights granted to Bayer under this Agreement, and has not taken any action that would in any way prevent it from granting the rights granted to Bayer under this Agreement, or that would otherwise materially conflict with or adversely affect Bayer's rights under this Agreement;

11.2.7 Third Party Technology. To Dimension's knowledge, (i) the manufacture, development and Commercialization of Licensed GT Products, as contemplated by Dimension as of the Original Effective Date, will not infringe or misappropriate any intellectual property rights of a Third Party, and (ii) there are no pending Third Party patent applications that, if issued with the published or currently pending claims, would be infringed by the manufacture, development or Licensed GT Products or any components thereof, as contemplated by Dimension as of the Original Effective Date; provided, however, that Dimension makes no representation in this Section 11.2.7 with respect to any formulation or delivery system that may be used for a Licensed Treatment;

11.2.8 Third Party Infringement. To Dimension's knowledge as of the Original Effective Date, no Third Party is infringing or has infringed any Licensed Patents or has misappropriated any Licensed Know-How;

11.2.9 No Proceeding**.** There are no pending, or, to Dimension's knowledge, no threatened, adverse actions, suits or proceedings (including interferences, reissues, re-examinations, cancellations or oppositions) against Dimension involving the Licensed Patents;

11.2.10 ReGenX Agreement.

11.2.10.1 As of the Original Effective Date, Dimension represents and warrants to Bayer that it has provided to Bayer a true, correct and complete copy thereof, but for redaction of (a) the royalty rates, (b) any other payment amounts, (c) certain terms not essential in determining the extent of the grant of rights to Bayer hereunder or that Bayer, as a prudent pharmaceutical company, might reasonably consider relevant in determining whether to enter into this Agreement on the terms and conditions contained herein, as such agreement is in effect as of the Original Effective Date.

11.2.10.2 Dimension represents and warrants to Bayer that, as of the Original Effective Date the ReGenX Agreement is in full force and effect, and that Dimension is not in breach of, nor do any circumstances exist upon which ReGenX might claim that Dimension is in breach of, the ReGenX Agreement; provided, however, despite Dimension's material compliance with the ReGenX Agreement, certain provisions under this Agreement, including without limitation the timing provisions in Sections 6.5 and 9.5 and the definition in Section 9.7.3, are different from and not technically in compliance with the terms of the ReGenX Agreement, and accordingly, Bayer acknowledges and understands that any breach by Dimension, or termination by ReGenX, of the ReGenX Agreement resulting from such differences shall not constitute a breach of this Section 11.2.10.2 and of Section 11.2.10.3. For the avoidance of doubt, Dimension is not relieved of its obligations under this Agreement because compliance with or fulfillment of such obligations may give rise to a breach of the ReGenX Agreement.

11.2.10.3 As of the Original Effective Date, Dimension further covenants and agrees that (a) it will take all steps necessary to maintain in full force and effect, the ReGenX Agreement with respect to the Field for the term thereof (b) it will not assign (except to an Affiliate or an assignment to a Third Party to which this Agreement has been assigned as permitted under Section 13.2), amend, restate, terminate in whole or in part, or otherwise modify the ReGenX Agreement in any way that adversely affects Bayer's rights under this Agreement without the prior written consent of Bayer; (c) it will provide Bayer with prompt notice of any claim of a breach under the ReGenX Agreement or notice of termination of the ReGenX Agreement made by either Dimension or ReGenX (or any party acting on behalf of such counterparty) that relates to the Field; (d) it will promptly send to Bayer copies of all other material correspondence related to the Field to or from the counterparty to such ReGenX Agreement; and (e) it will enforce its rights under the ReGenX to the extent necessary to maintain Bayer's rights hereunder.

11.3 Mutual Covenants.

11.3.1 No Debarment. In the course of the development of Licensed GT Products and Licensed Treatments, neither Party shall use any employee or consultant who has been debarred by any regulatory authority or, to such Party's knowledge, is the subject of

debarment proceedings by a regulatory authority. Each Party shall notify the other Party promptly upon becoming aware that any of its employees or consultants who are involved with the development of Licensed GT Products and Licensed Treatments hereunder has been debarred or is the subject of debarment proceedings by any regulatory authority.

11.3.2 Compliance. Each Party and its Affiliates shall comply in all material respects with all applicable Laws in the development and Commercialization of GT Products, Licensed GT Products and Licensed Treatments and performance of its obligations under this Agreement, including, to the extent applicable to such Party and its activities hereunder, the statutes, regulations and written directives of the FDA, the EMA and any regulatory authority having jurisdiction in the Territory, the FD&C Act, the Prescription Drug Marketing Act, the Federal Health Care Programs Anti-Kickback Law, 42 U.S.C. 1320a-7b(b), the statutes, regulations and written directives of Medicare, Medicaid and all other health care programs, as defined in 42 U.S.C. § 1320a-7b(f), and the Foreign Corrupt Practices Act of 1977, each as may be amended from time to time.

11.4 Disclaimer of Warranties, Damages. EXCEPT AS SET FORTH IN SECTIONS 11.1 AND 11.2, THE DIMENSION POC TECHNOLOGY, LICENSED TECHNOLOGY, POC TRIAL MATERIAL, LICENSED GT PRODUCTS, LICENSED TREATMENTS, AND ALL RIGHTS LICENSED BY EITHER PARTY TO THE OTHER UNDER THIS AGREEMENT ARE PROVIDED ON AN "AS IS" BASIS, AND NEITHER PARTY MAKES ANY REPRESENTATIONS OR WARRANTIES, EXPRESS OR IMPLIED, WITH RESPECT THERETO. BY WAY OF EXAMPLE BUT NOT OF LIMITATION, EXCEPT AS SET FORTH IN SECTIONS 11.1 AND 11.2, NEITHER PARTY MAKES ANY REPRESENTATIONS OR WARRANTIES, AND HEREBY DISCLAIMS ALL EXPRESS AND IMPLIED REPRESENTATIONS AND WARRANTIES, (i) OF COMMERCIAL UTILITY, ACCURACY, COMPLETENESS, PERFORMANCE, MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, VALIDITY OR ENFORCEABILITY OF ANY RIGHTS LICENSED BY EITHER PARTY TO THE OTHER, AND PROFITABILITY; OR (ii) THAT THE USE OF ANY RIGHTS GRANTED BY EITHER PARTY TO THE OTHER, INCLUDING ANY PRODUCTS RESULTING THEREFROM, WILL NOT INFRINGE ANY PATENT, COPYRIGHT, TRADEMARK, OR OTHER PROPRIETARY RIGHTS OF THIRD PARTIES. EXCEPT AS SET FORTH IN THIS AGREEMENT, NEITHER PARTY OR ANY OF SUCH PARTY'S DIRECT OR INDIRECT LICENSORS SHALL BE LIABLE TO THE OTHER PARTY, ITS SUCCESSORS OR ASSIGNS, OR ANY SUBLICENSEES OF EITHER PARTY, OR ANY THIRD PARTY WITH RESPECT TO: (a) ANY CLAIM ARISING FROM USE OF ANY OR ALL RIGHTS LICENSED UNDER THIS AGREEMENT OR FROM THE DEVELOPMENT, TESTING, MANUFACTURE, USE, OR SALE OF PRODUCTS ARISING THEREFROM; OR (b) ANY CLAIM FOR LOSS OF PROFITS, LOSS OR INTERRUPTION OF BUSINESS, OR FOR INDIRECT, SPECIAL, INCIDENTAL, PUNITIVE, OR CONSEQUENTIAL DAMAGES OF ANY KIND, INCLUDING ANY ARISING FROM OR RELATING TO ANY BREACH OF THIS AGREEMENT OR THE EXERCISE OF RIGHTS HEREUNDER, REGARDLESS OF ANY NOTICE OF SUCH DAMAGES. NOTHING IN THIS SECTION 11.4 IS INTENDED TO LIMIT OR RESTRICT THE INDEMNIFICATION RIGHTS OR OBLIGATIONS OF EITHER PARTY UNDER SECTION 11.5 OR TO LIMIT A PARTY'S LIABILITY FOR BREACHES OF ITS OBLIGATION REGARDING CONFIDENTIALITY UNDER ARTICLE 8.

11.5 Indemnification.

11.5.1 By Bayer. Bayer shall defend, indemnify, and hold harmless Dimension, its Affiliates, ReGenX and the licensors under the Existing Licenses, and their respective shareholders, members, partners, officers, trustees, faculty, students, contractors, agents, and employees (individually, a "Dimension Indemnified Party" and, collectively, the "Dimension Indemnified Parties") from and against any and all Third Party liability, loss, damage, action, claim, fee, cost, or expense (including attorneys' fees) (individually, a "Third Party Liability" and, collectively, the "Third Party Liabilities") suffered or incurred by the Dimension Indemnified Parties from claims of such Third Parties that result from or arise out of: (i) the research, development, testing, use, manufacture, promotion, sale, or other disposition of any Dimension POC Technology, Licensed Technology, POC Trial Material, or Licensed GT Products by Bayer, its Affiliates, any Sublicensees, their respective assignees, or vendors acting on behalf of any of the foregoing; (ii) any breach by Bayer (or its Affiliates or any Sublicensees) of its representations, warranties, or obligations of this Agreement; and (iii) Bayer's gross negligence or intentional misconduct or that of Bayer's Affiliates or Sublicensees; provided, however, that Bayer shall not be liable for claims based on any breach by Dimension of its representations, warranties, or obligations of this Agreement or the gross negligence or intentional misconduct of any of the Dimension Indemnified Parties. Without limiting the foregoing, but subject to the proviso contained in the preceding sentence, Bayer must defend, indemnify, and hold harmless the Dimension Indemnified Parties from and against any Third Party Liabilities resulting from:

(a) any product liability or other claim of any kind related to the use by a Third Party of a Licensed GT Product that was manufactured, sold, or otherwise disposed of by Bayer, its Affiliates, any Sublicensees, their respective assignees, or vendors;

(b) any product liability or other claim of any kind related to the use of defective POC Trial Material, but solely to the extent the POC Trial Material is defective due to circumstances following delivery of the POC Trial Material to Bayer in accordance with that certain letter agreement by and between the Parties, dated May 23, 2018 (the "Letter Agreement")

(c) any claim by a Third Party that the practice of the Licensed Technology, or the design, composition, manufacture, use, sale, or other disposition of any Licensed Treatment infringes or violates any patent, copyright, trade secret, trademark, or other intellectual property right of such Third Party; and

(d) clinical trials or studies conducted by or on behalf of Bayer, its Affiliates, any Sublicensees, their respective assignees, or vendors relating to the Licensed Treatment or Licensed GT Products, including any claim by or on behalf of [***] of any such clinical trial or study.

For the avoidance of doubt, the indemnities granted by Bayer shall not apply in respect of any activities conducted following the exercise by Dimension of its rights under Section 9.9.4.

11.5.2 By Dimension. Dimension shall defend, indemnify, and hold harmless Bayer, its Affiliates and Sublicensees and their respective shareholders, members, partners, officers, trustees, contractors, agents, and employees (individually, a "Bayer Indemnified Party" and, collectively, the "Bayer Indemnified Parties") from and against any and all Third Party Liabilities suffered or incurred by the Bayer Indemnified Parties from claims of such Third Parties that result from or arise out of: (i) the research, development, testing, use, manufacture, promotion, sale, or other disposition of any GT Product, Compound/Vector or any product outside the Field or within the scope of the Retained Rights by Dimension, ReGenX or its Affiliates and their respective licensees or sublicensees, assignees, or vendors acting on behalf of any of the foregoing; (ii) supply by Dimension's contract manufacturer of defective POC Trial Material, but solely to the extent the POC Trial Material is defective due to circumstances prior to delivery of the POC Trial Material to Bayer in accordance with the Letter Agreement, (iii) any breach by Dimension (or its Affiliates) of its representations, warranties, or obligations of this Agreement; and (iv) Dimension's gross negligence or intentional misconduct or that of ReGenX or Dimension's or ReGenX's respective Affiliates, licensees and sublicensees; provided, however, that Dimension shall not be liable for claims based on any breach by Bayer of its representations, warranties, or obligations of this Agreement or the gross negligence or intentional misconduct of any of the Bayer Indemnified Parties.

11.5.3 Indemnification Procedure. Each Party, as an indemnifying party (an "Indemnifying Party"), shall not be permitted to settle or compromise any claim or action giving rise to Third Party Liabilities in a manner (i) that imposes any restrictions or obligations on the indemnified party (an "Indemnified Party") or, if Bayer is the Indemnifying Party, on ReGenX or its licensors under the Existing Licenses, without the other Party's prior written consent, (ii) if Bayer is the Indemnifying Party, that grants any rights to the Licensed Technology or Licensed GT Products other than those Bayer has the right to grant under this Agreement without Dimension's prior written consent, or (iii) if Dimension is the Indemnifying Party, that grants any rights that are inconsistent with those granted to Bayer under this Agreement without Bayer's prior written consent. The Indemnified Party shall notify the Indemnifying Party within [***] of becoming aware of any claim or claims asserted or threatened against the Indemnified Party that could give rise to a right of indemnification under this Agreement, *provided however* that the failure to give such notice shall not relieve the Indemnifying Party of its indemnity obligation hereunder except to the extent that such failure materially prejudices its rights hereunder. The Indemnifying Party shall be permitted to control any litigation or potential litigation involving the defense of any claim subject to indemnification pursuant to this Section 11.5, including the selection of counsel. The Indemnified Party shall keep the Indemnifying Party apprised of all material developments with respect to the claim and promptly provide the Indemnifying Party with copies of all correspondence and documents exchanged by the Indemnified Party and the opposing party(ies) to such litigation. The Indemnified Party may not compromise or settle such litigation without the prior written consent of the Indemnifying Party, such consent not to be unreasonably withheld or delayed. The indemnification rights of a Indemnified Party contained in this Agreement are in addition to all other rights which such Indemnified Party may have at law or in equity or otherwise. The Indemnifying Party will pay directly all Third Party Liabilities incurred for defense or negotiation of any claim hereunder or will reimburse the Indemnified Party for all documented Third Party Liabilities incident to the defense or negotiation of any such claim within [***] after the Indemnifying Party's receipt of invoices for such fees, expenses, and charges.

11.6 Insurance. Within [***] of the Original Effective Date, each Party will procure and maintain product liability insurance policies during the term of the Agreement for claims related to bodily injury or death caused by the Licensed GT Products. In lieu of insurance coverage described in the preceding sentence, Bayer shall have the right to undertake a program of self-insurance to cover the obligations hereunder, with financial protection comparable to that arranged by it for its own protection with regard to other products in its portfolio. Prior to [***], and thereafter for a period required by applicable Law in order to continue to monitor the participants in the clinical trial, clinical trials coverage will be arranged in amounts that are reasonable and customary in the location where such clinical trial is being conducted. Such insurance coverage will be arranged by Dimension if it is the sponsor of the applicable clinical trial and shall be arranged by Bayer if it is the sponsor of the applicable clinical trial.

ARTICLE 12: USE OF NAME

Except as permitted by this Agreement, Bayer, its Affiliates, any Sublicensees, and all of its and their employees and agents must not use ReGenX's and, to the extent relating to the subject matter of this Agreement, the University of Pennsylvania's and SmithKline Beecham Corporation's, name, seal, logo, trademark, or service mark (or any adaptation thereof) or the name, seal, logo, trademark, or service mark (or any adaptation thereof) of any of such entities' representative, school, organization, employee, or student in any way without the prior written consent of Dimension or such entity, as applicable; provided, however that Bayer may acknowledge the existence and general nature of this Agreement. The foregoing limitations shall apply *mutatis mutandis*, to Dimension's use of Bayer's or its Affiliates or Sublicensees name, logo, seal, trademark or service marks.

ARTICLE 13: ADDITIONAL PROVISIONS

13.1 Relationship. Nothing in this Agreement shall be deemed to establish a relationship of principal and agent between Bayer and Dimension, nor any of their agents or employees for any purpose whatsoever, nor shall this Agreement be construed as creating any other form of legal association or arrangement which would impose liability upon one Party for the act or failure to act of the other Party.

13.2 Assignment. Subject to Sections 13.2.1 through 13.2.6 below, this Agreement will be binding upon and inure to the benefit of the Parties hereto and their respective successors and permitted assigns, each of which such successors and permitted assigns will be deemed to be a Party hereto for all purposes hereof.

13.2.1 Subject to Section 13.2.2 and 13.2.3, no Party may assign, delegate or otherwise transfer either this Agreement or any of its rights, interests, or obligations hereunder without the prior written approval of the other Party.

13.2.2 Notwithstanding Section 13.2.1 each Party, upon providing the other Party written notice, may without the consent of the other Party, (i) assign any or all of its rights and interests hereunder to one or more of its Affiliates, (ii) designate one or more of its Affiliates to perform its obligations hereunder, in each case, so long as the assigning Party is not relieved of any liability hereunder and so long as any such Affiliate remains such Party's Affiliate;

provided, however, that such Affiliate assignee(s) provide the other Party with written acknowledgement of and agreement to the assigning Party's obligations under the Agreement that were assigned to it.

13.2.3 Notwithstanding Section 13.2.1 each Party (or its permitted successive assignees or transferees hereunder), upon providing the other Party prior written notice (at least [***] prior to the effectiveness of such assignment), may without the consent of the other Party, assign or transfer this Agreement as a whole to an entity that succeeds to all or substantially all of the business or assets of such Party related to the subject matter of this Agreement, so long as the assigning Party is not relieved of any liability hereunder and such assignment is a Qualified Assignment.

13.2.4 For the purposes of this Agreement, a "Qualified Assignment" means any transaction that:

(a) is made in compliance with Law, including securities, tax and corporation laws;

(b) includes the assignee's written acknowledgement (to the assigning Party) of and agreement to assume all of the assigning Party's obligations under the Agreement;

(c) is made to an assignee that is, and will be after giving effect to the relevant assignment, Solvent;

(d) is made to an assignee that is not subject at the time of such assignment to any order, decree or petition providing for (i) the winding-up or liquidation of such person, (ii) the appointment of a receiver over the whole or part of the assets of such person or (iii) the bankruptcy or administration of such person;

(e) is not a voidable fraudulent conveyance;

(f) is made to an assignee that is at the time of such assignment not debarred under 21 U.S.C. §30 or under investigation or threatened to be debarred under 21 U.S.C. §30; and

(g) will not cause a material increase in taxes, costs or expenses to the non-assigning Party (unless the assigning Party or the assignee has agreed to compensate the non-assigning Party for the same).

13.2.5 Notwithstanding Sections 13.2.1 through 13.2.4 above, (i) each Party may at any time assign its rights, interests and obligations provided for hereunder to any person by merger or in the course of a Change of Control; or (ii) with the prior written consent of the other Party.

13.2.6 For purposes of this Section 13.2, "Solvent" means, with respect to any entity as on any date of determination, that as of such date, (i) the value of the assets of such entity is greater than the total amount of liabilities (including contingent and unliquidated liabilities) of such entity, (ii) such entity is able to pay all liabilities of such entity as such

liabilities mature and (iii) such entity does not have unreasonably small capital (taking into account such entity's obligations hereunder). In computing the amount of contingent or unliquidated liabilities at any time, such liabilities shall be computed at the amount that, in light of all the facts and circumstances existing at such time, represent the amount that can reasonably be expected to become an actual or matured liability. In computing the value of the assets of an entity, the value shall be determined in the context of current facts and circumstances affecting such entity.

13.3 Waiver. A waiver by either Party of a breach of any provision of this Agreement will not constitute a waiver of any subsequent breach of that provision or a waiver of any breach of any other provision of this Agreement.

13.4 Notices. Notices, payments, statements, reports, and other communications under this Agreement shall be in writing and shall be deemed to have been received as of the date received if sent by public courier (*e.g.*, Federal Express), by Express Mail, receipt requested, or by facsimile (with a copy of such facsimile also sent by one of the other methods of delivery) and addressed as follows:

If for Dimension:	with a copy (which shall not constitute notice) to:
Ultragenyx Pharmaceutical Inc. 60 Leveroni Court Novato, CA 94949 Attn: SVP, Business Development and Alliance Management	Ultragenyx Pharmaceutical Inc. 60 Leveroni Court Novato, CA 94949 Attn: General Counsel
If for Bayer:	with a copy to:
Bayer HealthCare LLC 455 Mission Bay Boulevard South San Francisco, CA 94158 Attn: Alliance Manager Facsimile: [***]	Bayer HealthCare LLC 800 Dwight Way Berkeley, CA 94710 Attn: Law & Patents

Either Party may change its official address upon written notice to the other Party.

13.5 Applicable Law. This Agreement shall be construed and governed in accordance with the laws of the State of New York, without giving effect to conflict of law provisions that may require the application of the laws of another jurisdiction. Subject to Section 13.6, the Parties hereby submit to the exclusive jurisdiction of and venue in the federal courts located in the State of New York with respect to any and all disputes concerning the subject of this Agreement.

13.6 Dispute Resolution. In the event of any controversy or claim arising out of or relating to this Agreement, the Parties shall first attempt to resolve such controversy or claim through good faith negotiations between senior executives of each Party with authority to resolve the dispute for a period of not less than [***] following notification of such controversy or claim

to the other Party. If such controversy or claim cannot be resolved by means of such negotiations during such period, then such controversy or claim shall be resolved by binding arbitration administered by the American Arbitration Association ("AAA") in accordance with the Commercial Arbitration Rules of the AAA (including the ICDR Rules relating to discovery) in effect on the date of commencement of the arbitration, subject to the provisions of this Section 13.6. The arbitration shall be conducted as follows:

13.6.1 The arbitration shall be conducted by three arbitrators, each of whom by training, education, or experience has knowledge of the research, development, and commercialization of biological therapeutic products in the United States. The arbitration shall be conducted in English and held in New York, New York.

13.6.2 In its demand for arbitration, the Party initiating the arbitration shall provide a statement setting forth the nature of the dispute, the names and addresses of all other parties, an estimate of the amount involved (if any), the remedy sought, otherwise specifying the issue to be resolved, and appointing one neutral arbitrator. In an answering statement to be filed by the responding Party within [***] after confirmation of the notice of filing of the demand is sent by the AAA, the responding Party shall appoint one neutral arbitrator. Within [***] from the date on which the responding Party appoints its neutral arbitrator, the first two arbitrators shall appoint a chairperson.

13.6.3 If a Party fails to make the appointment of an arbitrator as provided in Section 13.6.2, the AAA shall make the appointment. If the appointed arbitrators fail to appoint a chairperson within the time specified in Section 13.6.2 and there is no agreed extension of time, the AAA shall appoint the chairperson.

13.6.4 The arbitrators will render their award in writing and, unless all Parties agree otherwise, will include an explanation in reasonable detail of the reasons for their award. Judgment upon the award rendered by the arbitrators may be entered in any court having jurisdiction thereof, including in the courts described in Section 13.5. The arbitrators will have the authority to grant injunctive relief and other specific performance; provided that the arbitrators will have no authority to award damages in contravention of this Agreement, and each Party irrevocably waives any claim to such damages in contravention of this Agreement. The arbitrators will, in rendering their decision, apply the substantive law of the State of New York, without giving effect to conflict of law provisions that may require the application of the laws of another jurisdiction. The decision and award rendered by the arbitrators will be final and non-appealable (except for an alleged act of corruption or fraud on the part of the arbitrator).

13.6.5 The Parties shall use their reasonable efforts to conduct all dispute resolution procedures under this Agreement as expeditiously, efficiently, and cost-effectively as possible.

13.6.6 All expenses and fees of the arbitrators and expenses for hearing facilities and other expenses of the arbitration will be borne equally by the Parties unless the Parties agree otherwise or unless the arbitrators in the award assess such expenses against one of the Parties or allocate such expenses other than equally between the Parties. Each of the Parties

will bear its own counsel fees and the expenses of its witnesses except to the extent otherwise provided in this Agreement or by applicable Law.

13.6.7 Compliance with this Section 13.6 is a condition precedent to seeking relief in any court or tribunal in respect of a dispute, but nothing in this Section 13.6 will prevent a Party from seeking equitable or other interlocutory relief in the courts of appropriate jurisdiction, pending the arbitrators' determination of the merits of the controversy, if applicable to protect the confidential information, property, or other rights of that Party or to otherwise prevent irreparable harm that may be caused by the other Party's actual or threatened breach of this Agreement.

13.7 No Discrimination. Both Parties and their respective Affiliates, and any Sublicensees, agents, contractors and licensees, in their respective activities under this Agreement, shall not discriminate against any employee or applicant for employment because of race, color, sex, sexual, or affectional preference, age, religion, national, or ethnic origin, handicap, or because he or she is a disabled veteran or a veteran (including a veteran of the Vietnam Era).

13.8 Compliance with Law. Both Parties (and their respective Affiliates and any Sublicensees, agents, contractors and licensees) must comply with all prevailing laws, rules, and regulations that apply to its activities or obligations under this Agreement. Without limiting the foregoing, it is understood that this Agreement may be subject to United States laws and regulations controlling the export of technical data, computer software, laboratory prototypes, and other commodities, articles, and information, including the Arms Export Control Act as amended in the Export Administration Act of 1979 and that Bayer's obligations are contingent upon compliance with applicable United States export laws and regulations. The transfer of certain technical data and commodities may require a license from the cognizant agency of the United States Government and/or written assurances by Bayer that Bayer shall not export data or commodities to certain foreign countries without prior approval of such agency. Dimension neither represents that a license is not required nor that, if required, it will issue.

13.9 Entire Agreement. This Agreement embodies the entire understanding between the Parties relating to the subject matter hereof and supersedes all prior understandings and agreements, whether written or oral. All "Confidential Information" disclosed by Dimension to Fidelity Biosciences Corp. (and then disclosed by Fidelity Biosciences Corp. to Bayer) pursuant to that certain Confidentiality Agreement dated September 10, 2012 between Dimension and Fidelity Biosciences Corp. or pursuant to any other agreements between them will be deemed "Confidential Information" under this Agreement (unless and until it falls within one of the exclusions set forth in Section 1.11). For the avoidance of doubt, this Agreement amends and restates the Original Agreement and the Original Agreement shall be of no force or effect as of the A&R Effective Date. This Agreement may not be varied except by a written document signed by duly authorized representatives of both Parties.

13.10 Marking. Bayer, its Affiliates, and any Sublicensees shall mark any POC Trial Material and any Licensed GT Product (or their containers or labels) made, sold, or otherwise distributed by it or them with any notice of patent rights necessary or desirable under applicable Law to enable the Dimension POC Technology, Sublicensed Patents and Dimension Patents to

be enforced to their full extent in any country where POC Trial Material or Licensed GT Products are made, used, sold, offered for sale, or imported.

13.11 Severability and Reformation. If any provision of this Agreement is held to be invalid or unenforceable by a court of competent jurisdiction, then such invalid or unenforceable provision will be automatically revised to be a valid or enforceable provision that comes as close as permitted by law to the Parties' original intent; provided that, if the Parties cannot agree upon such valid or enforceable provision, the remaining provisions of this Agreement will remain in full force and effect, unless the invalid or unenforceable provisions are of such essential importance to this Agreement that it is to be reasonably assumed that the Parties would not have entered into this Agreement without the invalid or unenforceable provisions.

13.12 Further Assurances. Each Party hereto agrees to execute, acknowledge, and deliver such further instruments, and to do all other acts, as may be necessary or appropriate in order to carry out the purposes and intent of this Agreement.

13.13 Interpretation; Construction. The captions to the several Articles and Sections of this Agreement are included only for convenience of reference and shall not in any way affect the construction of, or be taken into consideration in interpreting, this Agreement. In this Agreement, unless the context requires otherwise, (a) the word "including" shall be deemed to be followed by the phrase "without limitation" or like expression; (b) references to the singular shall include the plural and vice versa; (c) references to masculine, feminine, and neuter pronouns and expressions shall be interchangeable; (d) the words "herein" or "hereunder" relate to this Agreement; (e) "or" is disjunctive but not necessarily exclusive; (f) the word "will" shall be construed to have the same meaning and effect as the word "shall"; (g) all references to "dollars" or "$" herein shall mean U.S. Dollars; (h) unless otherwise provided, all reference to Sections and exhibits in this Agreement are to Sections and exhibits of and in this Agreement; and (i) whenever this Agreement refers to a number of days, such number shall refer to calendar days unless business days are specified. 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 provisions.

13.14 Cumulative Rights and Remedies. The rights and remedies provided in this Agreement and all other rights and remedies available to either Party at law or in equity are, to the extent permitted by law, cumulative and not exclusive of any other right or remedy now or hereafter available at law or in equity. Neither asserting a right nor employing a remedy shall preclude the concurrent assertion of any other right or employment of any other remedy, nor shall the failure to assert any right or remedy constitute a waiver of that right or remedy.

13.15 Counterparts. This Agreement may be executed in one or more counterparts, each of which will be deemed an original, but all of which together will constitute one and the same instrument.

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IN WITNESS WHEREOF, the Parties, intending to be legally bound, have caused this Collaboration and License Agreement to be executed by their duly authorized representatives.

ULTRAGENYX PHARMACEUTICAL INC.	BAYER HEALTHCARE LLC
By: /s/ Karah Parschauer	By: /s/ Chris Haskell
Name: Karah Parschauer	Name: Chris Haskell
Title: VP & Secretary	Title: VP and Site Head of West Coast Innov. Center

Exhibit A
Sublicensed Patents & Dimension Patents

Sublicensed Patents:

App #	Title	Inventors	Nos.	Penn Docket #
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]

Dimension Patents: [***]

Exhibit B
Licensed Treatment Sales

The following are examples (not intended to be exhaustive) of the calculation of Licensed Treatment Sales. In principle the Parties have agreed upon two payment mechanisms for the commercialization of Licensed Treatments; these are:

1. Annuity Payment Scheme (the figures mentioned below are hypothetical and do not reflect actual or anticipated prices):

   - [***]
   - [***]
   - [***]
   - [***]
   - [***]

   Table 1: [***] (which rolls up into the definition of Net Sales) for purposes of determining royalty payments to Dimension in relation to the amount of [***]– figures picked at random (and represent an example only):

Retail price of [***] (as a % of Licensed Treatment Monitoring Sales for such patient)	**% of [***] Licensed Treatment Monitoring Sales to be included in Licensed Treatment Sales/Net Sales for royalty purposes**
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]

2. One-time (lump sum) Payment Scheme:

   - [***]
   - [***]
   - [***]
   - [***]

Exhibit C
Sublicensed Technology Retained Rights

Bayer acknowledges and understands that ReGenX and its direct and indirect licensors under the Existing Licenses retain certain rights under the Sublicensed Technology, whether inside or outside the Field, as further set forth below:

1. Retained Rights. ReGenX's direct and indirect licensors retain the following rights with respect to the Sublicensed Technology:

   (a) A non-exclusive, sublicensable right under the Sublicensed Technology to make, have made, use, sell, offer to sell, and import products that deliver RNA interference and antisense drugs using an adeno-associated vector; and

   (b) A non-exclusive right for ReGenX's direct and indirect licensors (which right is sublicensable by such licensors) to use the Sublicensed Technology for non-commercial research purposes and to use the Sublicensed Technology for such licensors' discovery research efforts with non-profit organizations and collaborators.

2. Domain Antibodies. The rights and licenses granted in Section 5.1 shall not include any right (and Dimension's direct and indirect licensors retain the exclusive (even as to Dimension and Bayer), fully sublicensable right) under the Sublicensed Technology to make, have made, use, sell, offer to sell, and import Domain Antibodies (as defined in the ReGenX Agreement) that are expressed by an adeno-associated vector.

3. Hemophilia B.

   a. The rights and licenses granted in Section 5.1 shall not include any right (and ReGenX's direct and indirect licensors retain the exclusive (even as to Dimension and Bayer), fully sublicensable right) under the Sublicensed Technology that covers the rAAV serotype 8, to make, have made, use, sell, offer for sale, and import products for the treatment of all forms of hemophilia B (notwithstanding Bayer's rights under Section 5.12).

   b. ReGenX's direct and indirect licensors retain the following rights (even as to Dimension) with respect to the Sublicensed Technology: a non-exclusive, sublicensable right to make, have made, use, sell, offer for sale, and import all of the various serotypes of any adeno-associated vector that is the subject of at least one claim in the Sublicensed Patents solely for non-commercial research in the area of hemophilia B (notwithstanding Bayer's rights under Section 5.12).

4. Hemophilia A. ReGenX's direct and indirect licensors retain the following rights with respect to the Sublicensed Technology: to the extent Sublicensed Technology pertains to recombinant adeno-associated virus serotype 8, an exclusive, sublicensable right to make, have made, use, sell, offer for sale, and import products for the treatment of hemophilia A.

5. Service Businesses. The rights and licenses granted in Section 5.1 shall not include any right (and ReGenX's direct and indirect licensors retain the exclusive (even as to Dimension and Bayer), fully sublicensable right) under the Sublicensed Technology:

(a) to conduct commercial reagent and services businesses, which includes the right to make, have made, use, sell, offer to sell, and import research reagents, including any viral vector construct; provided that, for clarity, such rights retained by ReGenX's direct and indirect licensors shall not include the right to conduct clinical trials in humans in the Field; or

(b) to use the Sublicensed Technology to provide services to any Third Parties; provided that, for clarity, Bayer's license under Section 5.1 does include the right to administer Licensed GT Products to patients.

6. Research Rights. ReGenX's direct and indirect licensors retain the fully sublicensable right under the Sublicensed Technology to grant non-exclusive research and development licenses to their Affiliates and Third Parties; provided that such development rights granted by ReGenX's direct and indirect licensors shall not include the right to conduct clinical trials in humans in the Field or any rights to sell products in the Field.

7. Non-Commercial Entities. The University of Pennsylvania may use and permit other non-profit organizations or other non-commercial entities to use the Sublicensed Technology solely for educational, research, and other non-commercial purposes.

Exhibit D-1
Research Plan

[see attached]

Exhibit D-2
Operating Plan

[see attached]

Exhibit D-3
Research Budget

[see attached]

Exhibit D-4
Regulatory and Manufacturing Support

[see attached]

Exhibit E
Demonstration of Clinical POC

The Clinical Proof of Concept will be considered having been achieved when all of the following criteria are met:

- Efficacy and Safety
    - [***]
    - [***]
    - [***]
- Pre-existing antibodies against [***]
    - [***]
    - [***]
- Feasibility of highest dose level tested
    - [***]

Exhibit F

Press Releases

[see attached]

Exhibit G

Transition Plan

Function	Activity	Projected Completion Date*
Regulatory	[***]	[***] [***]
CMC	[***]	[***]
Pharmaceutical Development	[***]	[***]
Nonclinical	[***]	[***]

Exhibit 10.3

ADDENDUM 6 TO LEASE DATED JULY 1, 2011

BY AND BETWEEN ULTRAGENYX PHARMACEUTICAL, INC. AS LESSEE AND

CONDIOTTI ENTERPRISES, INC. AS LESSOR

On or about July 1, 2011 Lessor and Lessee entered into a lease and Addendum 1 for approximately 19,916 square feet, comprising the entire second floor of the Premises located at 60 Leveroni Court, Novato, California. Subsequent to the execution of that Lease, the parties have executed Addenda two through five (together, the "Lease"), which, in addition to such other terms and conditions agreed to facilitate operation of the Lease and the subject changes, have extended the term of the Lease to 4/30/19 and expanded the space to include all of the Premises at 60 Leveroni Court (approximately 43,517 sf) and all of the Premises at 52 Leveroni Court (approximately 20,343 sf) and the first floor of the Premises located at 68 Leveroni Court (approximately 10,408 sf), bringing the total square footage subject to the Lease and Addenda to approximately 74,268 square feet.

Now, therefore, the parties wish to further amend the Lease according to the terms of this Addendum.

106. Section 51 of the Lease, Section 91 of Addendum 4 and Section 103 of Addendum 5 are hereby deleted.

107. The parties agree to extend the Term of the Lease to expire on December 31, 2024.

108. Base Monthly Rent for the period May 1, 2019 through December 31, 2019 shall be at $111,034.40. Thereafter, Base Monthly Rent shall be adjusted annually according to the Terms of the Lease.

109. The Letter of Credit # SVBSF006932 shall remain in full force and effect in the amount of $190,518.00 throughout the remaining Term of this Lease and any extensions thereof. This Letter of Credit is accepted in lieu of a cash Security Deposit and is intended to secure Lessee's full and faithful performance of the Lease.

110. So long as Lessee is not in Default of the Lease, Lessee shall have two consecutive Options to Extend the Lease Term for a period of five years each, subject to the following terms:

a.) The Options to Extend are personal to Lessee and are neither transferrable nor assignable to any other party;

b.) Lessee shall provide Lessor with not less than six months advance written notice of intent to exercise the Option to Extend. Should Lessor not receive such timely written notification, then the Option(s) to Extend shall expire.

c.) The Options to Extend shall be consecutive to this extended term. If the first Option is not exercised, then both Options to Extend shall expire.

d.) The first year (12 months) of the Option term(s) shall be at the same Base Monthly Rent as the expiring 12 month period, where such Base Monthly Rent was for the identical space;

e.) Thereafter, the Base Monthly Rent shall be increased annually per the terms of Section 8 of the Lease.

f.) Each party shall bear the costs of any commission , fees, or consulting incurred for such extension.

g.) Lessee shall retain all of the space currently indicated above and any further expansions executed on an "As-Is" basis without further allowance for Tenant Improvements.

111. Except as expressly modified by this Addendum 6 the Lease shall remain in full force and effect.

Agreed to this 29th day of April, 2019.

Lessee	Lessor
By: /s/ Thomas Kassberg	/s/ Jan Warz
Name: Thomas Kassberg Title: Chief Business Officer Ultragenyx Pharmaceutical, Inc.	Jan Warz, COO Condiotti Enterprises, Inc.

May 16, 2017

Mr. Erik Harris

Re: Offer of Employment

Dear Erik,

On behalf of Ultragenyx Pharmaceutical Inc. (the "Company"), I am pleased to offer you the position of **Senior Vice President, Head of North American Commercial Operations,** on the following terms, commencing on June 26, 2017 "Hire Date".

You will be a regular, full-time, exempt employee of the Company. You will report directly to Jayson Dallas, Chief Commercial Officer, and will work at our facility located at Brisbane, CA.

Base Salary

The Company will pay you an initial base salary at a gross annual rate of $340,000, less payroll deductions and withholdings, on a bi-weekly basis. If your Hire Date is on or after January 1 and before October 1 of the calendar year, you will be eligible to be considered for a salary merit increase during the next calendar year's Annual Performance Review process. If your Hire Date is after September 30 of the calendar year, you will not be eligible to be considered for a salary merit increase until the second Annual Performance Review process that follows your Hire Date. The Annual Performance Review process generally takes place in the first quarter of the calendar year. Salary merit increases, if any, will be awarded at the Company's discretion on the basis of your performance, and will be prorated based on the number of months that you actually worked during the previous calendar year if your Hire Date is on or before September 30.

Sign-On Bonus

In addition, the company will provide you with a one-time sign-on bonus in the amount of $50,000, less any applicable withholdings, to be paid within 30 days following your start date. In the event that your employment is ended for any reason other than a layoff due to reduction in staff or reorganization within 12 months of your Hire Date, you agree to repay the Company the full amount of the sign-on bonus no later than the effective date of your termination. If you do not repay the full amount of the sign-on bonus within the specified time, you also agree to pay all costs reasonably incurred by Ultragenyx in connection with the collection of this amount, including reasonable attorney's fees.

Annual Bonus Program

You will also be eligible to participate in Ultragenyx's discretionary annual bonus program. The current target bonus opportunity for your position is 35% of your annual base salary. However, the actual amount of such bonus, if any, will be determined by the Company in its sole discretion based on the Company's achievement of the financial and other goals established for the year and the Company's assessment of your job performance for the year. You must commence your employment

by September 30 in order to be eligible for a bonus for the calendar year during which you were hired. If you join the Company between January 1 and September 30, you will be eligible for a pro-rated bonus for that calendar year. When bonuses are awarded, they typically are paid on or around March 15 of the following year. To encourage continued tenure with the Company and satisfactory or better performance after the end of the bonus performance year and through the bonus payment date, to be eligible for a bonus payment, you must remain an active employee of the Company through bonus payment date, and maintain satisfactory or better job performance through the bonus payment date.

Further details pertaining to the Annual Bonus Plan are attached.

New Hire Equity Awards

Subject to approval by the Board, under the Company's 2014 Incentive Plan (the "Plan"), the Company shall grant you an option to purchase up to 15,000 shares (the "Option") of the Company's Common Stock at fair market value as determined by the Compensation Committee as of the date of grant. The Option will be subject to the terms and conditions of the Plan and your grant agreement. Your grant agreement will include a four-year vesting schedule, under which 25 percent of your shares will vest on the first (1st) anniversary of the date of grant, and thereafter 1/48th of the Option shall vest and become exercisable each month until your Option is fully vested, in each case subject to your continued employment by the Company (or its subsidiaries).

Subject to the approval of the Compensation Committee, you will also receive a grant of 3,000 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.

Annual Equity Grant Program

You may also be considered for the Company's discretionary annual equity grant program based on the Company's assessment of your job performance. If your Hire date is on or after January 1 and before October 1, you will be eligible for a grant in the calendar year that follows, with the amount of such equity grant, if any, being determined by the Company in its sole discretion and prorated if your Hire Date is after January 1.

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 include medical, dental and vision insurance coverage. Coverage for these benefits begin on your Hire Date and upon completion of your enrollment in the plans. 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, a PPO, and a HDHP), a dental and vision plan, life/AD&D insurance, disability and voluntary insurance as well as a 401k retirement plan, with a company match of 3%. The Company will cover 90% of the benefit costs for employees and 75% of the benefits costs for eligible dependents. 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.

Your will accrue vacation time at the rate of three weeks (120 hours) per year, up to an accrual cap of 180 hours, under the terms of the Company's PTO policy. You will also be eligible for 5 paid sick days.

"At Will" Employment

Employment at Ultragenyx is on an "at-will" basis, meaning that you are free to end your employment at any time, with or without advance notice and for any reason or no reason at all, and that Ultragenyx likewise may end your employment, at any time, with or without advance notice and for any reason or no reason at all. In addition, your job duties, title, responsibilities, reporting structure, 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. No manager or employee of the Company (other than the CEO) has any authority to enter into any agreement for employment for any specified period of time or to make any agreement for employment other than an at-will employment relationship, and then only if the Company's CEO does so in a written agreement that is signed by both you and the CEO.

Compliance with Company Policies

As an employee of the Company, you will be expected to comply with the Company's personnel and other policies, and acknowledge in writing that you have read the Company's Employee Handbook, a copy of which you will receive during your new employee orientation.

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 me and discuss your plans in advance of providing such services for review and evaluation of its impact on your work at the Company and so that no problem later arises that could have been avoided from the outset.

Conditions

This offer, and any employment pursuant to this offer, is conditioned upon the following:

- You accepting and returning a signed original of this offer letter;
- Your consent to, and results satisfactory to the Company of, reference and background checks.

Furthermore, this offer, and any employment pursuant to this offer, is conditioned upon you reviewing and completing the following new hire documents that will be provided to you via a welcome email from our New Hire Onboarding team prior to your start date:

- A *Mutual Agreement to Arbitrate Claims* and *Confidential Information and Inventions Assignment Agreement* without modifications;

- The completion of an I-9 form within the legally required time period, which requires that you provide a specified document(s) proving your identity and legal authorization to work in the United States of America.

You are encouraged to discuss any of the referenced documents with your own advisor to the extent you desire.

No Conflicting Obligations

In your work for the Company, you will be expected not to use or disclose any confidential information, including trade secrets, of any former employer or other person to whom you have an obligation of confidentiality. Rather, you will be expected to use only that information which is generally known and used by persons with training and experience comparable to your own, which is common knowledge in the industry or otherwise legally in the public domain, or which is otherwise provided or developed by the Company. You agree that you will not bring onto Company premises any unpublished documents or property belonging to any former employer or other person to whom you have an obligation of confidentiality. By signing this letter or electronically accepting its terms and conditions, you are representing that you have disclosed to the Company any contract you have signed that may restrict your activities on behalf of the Company, and that you are under no obligations or commitments, whether contractual or otherwise, that are inconsistent with your obligations under this offer letter and resulting agreement, and that you have returned all property and confidential information belonging to any prior employer.

Entire Agreement

This offer letter, together with the accompanying Agreement for Protection of Company Information and Mutual Agreement to Arbitrate Claims, forms the complete and exclusive statement of your employment agreement with the Company. It supersedes any other agreements or promises made to you by anyone, whether oral or written. Changes in your employment terms, other than those changes expressly reserved to the Company's discretion in this letter, require a written modification signed by an officer of the Company.

Please sign and date this letter, and return them to me by May 19, 2017, if you wish to accept employment at the Company under the terms described above. This offer will expire if we have not received your signed offer letter by that time. If you accept our offer, but would like a different start date from the one in the first paragraph above, please contact me as soon as possible.

We look forward to working with you on developing treatment for many rare genetic diseases and hope you find your employment at Ultragenyx Pharmaceutical Inc. 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/ Bee Nguyen

Bee Nguyen
Executive Director, Human Resources

I accept and agree to employment with Ultragenyx on the terms and conditions above:

Signature: /s/ Erik Harris
Erik Harris

Dated: 5/19/2017

Exhibit 10.5

Ultragenyx Pharmaceutical

August 3, 2015

Erik Harris

Re: Addendum to Offer of Employment dated May 16, 2017

Dear Erik,

This addendum will supersede the equity grant section of the previously signed offer of employment dated May 16, 2017. The Company has increased your original option grant of 15,000 to 30,000 effective with the commencement of your employment with Ultragenyx.

New Hire Equity Awards

Subject to approval by the Board, under the Company's 2014 Incentive Plan (the "Plan"), the Company shall grant you an option to purchase up to 30,000 shares (the "Option") of the Company's Common Stock at fair market value as determined by the Compensation Committee as of the date of grant. The Option will be subject to the terms and conditions of the Plan and your grant agreement. Your grant agreement will include a four-year vesting schedule, under which 25 percent of your shares will vest on the first (1st) anniversary of the date of grant, and thereafter 1/48th of the Option shall vest and become exercisable each month until your Option is fully vested, in each case subject to your continued employment by the Company (or its subsidiaries).

Subject to the approval of the Compensation Committee, you will also receive a grant of 3000 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.

"At Will" Employment

Employment at Ultragenyx is on an "at-will" basis, meaning that you are free to end your employment at any time, with or without advance notice and for any reason or no reason at all, and that Ultragenyx likewise may end your employment, at any time, with or without advance notice and for any reason or no reason at all. In addition, your job duties, title, responsibilities, reporting structure, 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. No manager or employee of the Company (other than the CEO) has any authority to enter into any agreement for employment for any specified period of time or to make any agreement for employment other than an at-will employment relationship, and then only if the Company's CEO does so in a written agreement that is signed by both you and the CEO.

Warm Regards,

/s/ Bee Nguyen

Bee Nguyen
Executive Director, Human Resources

I accept the above offer:

Signature: /s/ Erik Harris Dated: August 8, 2017

Print Name: Erik Harris

Exhibit 10.6

Ultragenyx Pharmaceutical

June 19, 2019

Erik Harris

Re: Addendum No. 2 to Offer of Employment dated May 16, 2017

Dear Erik,

This is a second addendum ("Addendum No.2") to your original offer of employment dated May 16, 2017 (the "Offer Letter"), and will outline the terms and conditions of your appointment to Chief Commercial Officer, commencing on June 11, 2019. We are excited about the important contributions you can make by joining the Ultragenyx executive team and are confident that you will play a key role in our company's growth and success.

Except as expressly set forth herein, all provisions of the Offer Letter and its subsequent Addendum No.1 shall remain in full force and effect. In the event of conflict between the provisions in the Offer Letter or Addendum No. 1 and this Addendum No.2, the provisions of this Addendum No. 2 shall control.

You will continue to be a regular, full-time, exempt employee of the Company.

Compensation

The Company will pay you a base salary at a gross annual rate of $450,000, less payroll deductions and withholdings, on a bi-weekly basis. The Compensation Committee of the Board shall review your Base Salary at least annually.

Annual Bonus Program

You will also be eligible to participate in Ultragenyx's discretionary annual bonus program. The current target bonus opportunity for your position is 45% of your annual base salary. However, the actual amount of such bonus, if any, will be determined by the Company in its sole discretion based on the Company's achievement of the financial and other goals established for the year and the Company's assessment of your job performance for the year. When bonuses are awarded, they typically are paid on or around March 15 of the following year. To encourage continued tenure with the Company and satisfactory or better performance after the end of the bonus performance year and through the bonus payment date, to be eligible for a bonus payment, you must remain an active employee of the Company through bonus payment date, and maintain satisfactory or better job performance through the bonus payment date.

New Equity Awards

Subject to approval by the Board, under the Company's 2014 Incentive Plan (the "Plan"), the Company shall grant you an option to purchase 12,000 shares (the "Option") of the Company's

Common Stock at fair market value as determined by the Compensation Committee as of the date of grant. The Option will be subject to the terms and conditions of the Plan and your grant agreement. Your grant agreement will include a four-year vesting schedule, under which 25 percent of your shares will vest on the first (1st) anniversary of the date of grant, and thereafter 1/48th of the Option shall vest and become exercisable each month until your Option is fully vested, in each case subject to your continued employment by the Company (or its subsidiaries).

Subject to the approval of the Compensation Committee, you will also receive a grant of 3,500 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.

Subject to the approval of the Compensation Committee, you will also receive a grant of 3,500 performance stock units (the "PSUs") pursuant to the Plan. The PSUs will vest 33% upon confirmation of the performance metric by the Compensation Committee, and 67% will vest on the first anniversary of the confirmation, in each case subject to your continued employment by the Company (or its consolidated subsidiaries). The PSUs shall be governed by the Company's standard form of performance stock unit agreement and the Plan.

Change of Control

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 18 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 l(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.

"At Will" Employment

Employment at Ultragenyx is on an "at-will" basis, meaning that you are free to end your employment at any time, with or without advance notice and for any reason or no reason at all, and that Ultragenyx likewise may end your employment, at any time, with or without advance notice and for any reason or no reason at all. The use and definitions of the terms "Cause," and "Constructive Termination" are for purposes of determining eligibility for and repayment of benefits identified in this offer letter, and do not alter the at-will nature of the employment relationship. In addition, your job duties, title, responsibilities, reporting structure, 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. No manager or employee of the Company (other than the CEO)

has any authority to enter into any agreement for employment for any specified period of time or to make any agreement for employment other than an at-will employment relationship, and then only if the Company's CEO does so in a written agreement that is signed by both you and the 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) willful engagement in conduct that is materially injurious to the Company, or otherwise in breach of your fiduciary duties

to the Company, after notice from the Board and a reasonable opportunity to cure of no less than thirty (30) days (if reasonably curable); (ii) conviction of, or plea of guilty or no contest to, any felony; (iii) any act of fraud or embezzlement by you with respect to your obligations or otherwise relating to the business of the Company; (iv) your willful refusal to implement or follow a lawful policy or directive (including without limitation, your failure to cooperate in any Company investigation) after notice from the Board and a reasonable opportunity to cure of no less than thirty (30) days (if reasonably curable); (v) your material breach of any agreement entered into between you and the Company; or (vi) 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-l(b)(4), 1.409A-l(b)(S) and l.409A-l(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 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.

Entire Agreement

This addendum, together with the Offer Letter and Addendum No. 1, forms the complete and exclusive statement of your employment agreement with the Company. It supersedes any other agreements or promises made to you by anyone, whether oral or written. Changes in your employment terms, other than those changes expressly reserved to the Company's discretion in this letter, require a written modification signed by an officer of the Company.

Warm Regards,

/s/ Emil D. Kakkis

Emil D. Kakkis, M.D., Ph.D. Chief
Executive Officer

I accept and agree to employment with Ultragenyx on the terms and conditions above:

Signature: /s/ Erik Harris Dated: July 3, 2019

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 1, 2019

/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 1, 2019

/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, 2019 (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 1, 2019

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

Dated: August 1, 2019

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