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 March 31, 2014

OR

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

For the transition period from _____ to _____.

Commission File No. 001-36276

ULTRAGENYX PHARMACEUTICAL INC.

(Exact name of registrant as specified in its charter)

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

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

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

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

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

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

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

As of May 7, 2014, the registrant had 30,035,894 shares of common stock issued and outstanding.

ULTRAGENYX PHARMACEUTICAL INC.

FORM 10-Q FOR THE QUARTER ENDED MARCH 31, 2014

INDEX

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

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

- our expectations regarding the timing of commencing our clinical studies and reporting results from same;
- the timing and likelihood of regulatory approvals for our product candidates;
- the potential market opportunities for commercializing our product candidates;
- our expectations regarding the potential market size and the size of the patient populations for our product candidates, if approved for commercial use;

estimates of our expenses, future revenue, capital requirements, and our needs for additional financing;

- our ability to develop, acquire, and advance product candidates into, and successfully complete, clinical studies;
- the implementation of our business model and strategic plans for our business and product candidates;
- the initiation, timing, progress, and results of future preclinical studies and clinical studies, and our research and development programs;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates;
- our ability to maintain and establish collaborations or obtain additional funding;
- our ability to maintain and establish relationships with third parties, such as contract research organizations, suppliers and distributors;
- our expectations regarding the time during which we will be an emerging growth company under the JOBS Act;
- our financial performance and expansion of our organization;
- our ability to obtain supply of our product candidates;
- developments and projections relating to our competitors and our industry; and
- other risks and uncertainties, including those listed under Part II, Item 1A. Risk Factors.

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

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

ULTRAGENYX PHARMACEUTICAL INC.
(A Development Stage Company)
CONDENSED BALANCE SHEETS
(In thousands, except share and per share amounts)

	March 31, 2014	December 31, 2013
	(Unaudited)	
Assets		
Current assets:		
Cash and cash equivalents	$ 55,447	$ 7,427
Short-term investments	109,950	45,950
Prepaid expenses and other current assets	4,239	1,848
Total current assets	169,636	55,225
Property and equipment, net	1,777	1,325
Restricted cash	744	451
Other assets	550	2,648
Total assets	$ 172,707	$ 59,649
Liabilities, Convertible Preferred Stock and Stockholders' Equity (Deficit)		
Current liabilities:		
Accounts payable	$ 3,495	$ 1,437
Accrued liabilities	3,238	4,406
Deferred rent—current portion	78	78
Total current liabilities	6,811	5,921
Convertible preferred stock warrant liability	—	3,419
Other liabilities	182	200
Total liabilities	6,993	9,540
Commitments and contingencies (Note 10)	—	—
Series A redeemable convertible preferred stock, par value of $0.001 per share—nil and 35,377,566 shares authorized; nil and 34,349,894 shares issued and outstanding as of March 31, 2014 and December 31, 2013	—	51,001
Series B convertible preferred stock, par value of $0.001 per share—nil and 27,081,680 shares authorized, issued and outstanding as of March 31, 2014 and December 31, 2013	—	73,929
Stockholders' equity (deficit):		
Preferred stock, par value of $0.001 per share—25,000,000 shares authorized; nil outstanding as of March 31, 2014 and December 31, 2013	—	—
Common stock, par value of $0.001 per share—250,000,000 shares authorized; 30,049,650 and 3,766,289 shares issued and outstanding as of March 31, 2014 and December 31, 2013	30	4
Additional paid-in capital	258,599	—
Accumulated other comprehensive income (loss)	(46)	11
Deficit accumulated during the development stage	(92,869)	(74,836)
Total stockholders' equity (deficit)	165,714	(74,821)
Total liabilities, convertible preferred stock and stockholders' equity (deficit)	$ 172,707	$ 59,649

See accompanying notes.

ULTRAGENYX PHARMACEUTICAL INC.
(A Development Stage Company)
CONDENSED STATEMENTS OF OPERATIONS
(Unaudited)
(In thousands, except share and per share amounts)

	Three Months Ended March 31,		Period from April 22, 2010 (Inception) Through March 31,
	2014	2013	2014
Operating expenses:			
Research and development	$ 8,353	$ 5,664	$ 54,499
General and administrative	1,986	1,083	11,916
Total operating expenses	10,339	6,747	66,415
Loss from operations	(10,339)	(6,747)	(66,415)
Other income (expense), net:			
Interest income	93	26	314
Interest expense	—	—	(318)
Other expense, net	(3,384)	(14)	(6,770)
Total other income (expense), net	(3,291)	12	(6,774)
Net loss	$ (13,630)	$ (6,735)	$ (73,189)
Net loss attributable to common stockholders	$ (18,438)	$ (8,205)	
Net loss per share attributable to common stockholders, basic and diluted	$ (0.85)	$ (2.84)	
Shares used in computing net loss per share attributable to common stockholders, basic and diluted	21,582,435	2,893,997	

See accompanying notes.

ULTRAGENYX PHARMACEUTICAL INC.
(A Development Stage Company)
CONDENSED STATEMENTS OF COMPREHENSIVE LOSS
(Unaudited)
(In thousands)

	Three Months Ended March 31,		Period from April 22, 2010 (Inception) Through March 31,
	2014	2013	2014
Net loss	$ (13,630)	$ (6,735)	$ (73,189)
Other comprehensive income:			
Unrealized loss on available-for-sale securities	(57)	—	(46)
Total comprehensive loss	$ (13,687)	$ (6,735)	$ (73,235)

See accompanying notes.

(A Development Stage Company)
CONDENSED STATEMENTS OF CASH FLOWS
(Unaudited)(In thousands)

	Three Months Ended March 31,		Period from April 22, 2010 (Inception) Through March 31,
	2014	2013	2014
Operating activities:			
Net loss	$ (13,630)	$ (6,735)	$ (73,189)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	117	124	914
Noncash interest expense	—	—	318
Amortization of premium (discount) on investment securities	479	(6)	1,892
Stock-based compensation	795	191	2,597
Revaluation of convertible preferred stock warrant liability	3,324	(2)	6,540
Changes in operating assets and liabilities:			
Prepaid expenses and other current assets	(2,391)	(776)	(4,239)
Other assets	2,098	(96)	(550)
Accounts payable	2,058	1,339	3,495
Accrued liabilities and other liabilities	(1,186)	(332)	3,498
Net cash used in operating activities	(8,336)	(6,293)	(58,724)
Investing activities:			
Purchase of property and equipment	(569)	(177)	(2,691)
Purchase of investments	(87,998)	(14,923)	(151,951)
Proceeds from maturities of investments	23,462	—	40,063
Increase in restricted cash	(293)	—	(744)
Net cash used in investing activities	(65,398)	(15,100)	(115,323)
Financing activities:			
Net proceeds from issuance of convertible preferred stock	—	—	103,888
Net proceeds from issuance of common stock	126,100	1	126,402
Proceeds from issuance of promissory notes	—	—	3,550
Payment of preferred stock dividend	(4,346)	—	(4,346)
Net cash provided by financing activities	121,754	1	229,494
Net increase (decrease) in cash and cash equivalents	48,020	(21,392)	55,447
Cash and cash equivalents at beginning of period	7,427	86,190	—
Cash and cash equivalents at end of period	$ 55,447	$ 64,798	$ 55,447
Supplemental disclosures of non-cash investing and financing information:			
Issuance of convertible preferred stock warrants	$ —	$ —	$ 202
Issuance of Series A redeemable convertible preferred stock in lieu of cash dividend	$ —	$ —	$ 2,070
Reclassification of warrant liability to equity upon conversion to common stock warrants	$ 6,743	$ —	$ 6,743
Conversion of interest accrued on promissory notes into Series A redeemable convertible preferred stock	$ —	$ —	$ 114
Conversion of promissory notes into Series A redeemable convertible preferred stock	$ —	$ —	$ 3,550
Conversion of Series A and Series B preferred stock to common stock	$ 129,360	$ —	$ 129,360

See accompanying notes.

1. Organization

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

The Company is focused on the identification, acquisition, development, and commercialization of novel products for the treatment of rare and ultra-rare diseases, with an initial focus on serious and debilitating metabolic genetic diseases. The Company is currently conducting a Phase 2 extension study of sialic acid, extended release (SA-ER) in patients with hereditary inclusion body myopathy (HIBM), a progressive muscle-wasting disorder; a Phase 1/2 study of recombinant human beta-glucuronidase (rhGUS) in patients with mucopolysaccharidosis 7, or MPS 7, a rare lysosomal storage disease; a Phase 2 clinical study for triheptanoin for the treatment of patients with glucose transporter type-1 deficiency syndrome (Glut1 DS), a brain energy deficiency; and a Phase 2 clinical study of triheptanoin, 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 also entered into a collaboration and license agreement with Kyowa Hakko Kirin Co., Ltd. (KHK) for KRN23, an antibody targeting fibroblast growth factor 23, or FGF23, intended for the treatment of X-linked hypophosphatemia, or XLH, a rare genetic disease that impairs bone growth.

On January 30, 2014, the Company's registration statements on Form S-1 (File Nos. 333-192244 and 333-193675) relating to its initial public offering (IPO) of its common stock were declared effective by the Securities and Exchange Commission (SEC). The shares began trading on The NASDAQ Global Select Market on January 31, 2014. The public offering price of the shares sold in the offering was $21.00 per share. The IPO closed on February 5, 2014 and included 6,624,423 shares of common stock, which included 864,054 shares of common stock issued pursuant to the over-allotment option granted to the underwriters. The Company received total proceeds from the offering of $129.4 million, net of underwriting discounts and commissions of $9.7 million. After deducting offering expenses of approximately $3.3 million and a cash dividend of $4.3 million, which was paid to the preferred stockholders on the closing date, net proceeds were approximately $121.7 million. Upon the closing of the IPO, all shares of convertible preferred stock then outstanding converted into 19,598,486 shares of common stock and the Series A convertible preferred stock warrants were converted into warrants to purchase common stock.

Upon the effectiveness of the Amended and Restated Certificate of Incorporation of the Company on February 5, 2014, the number of shares of capital stock the Company is authorized to issue was increased to 275,000,000 shares, of which 250,000,000 shares are common stock and 25,000,000 shares are preferred stock. Both the common stock and preferred stock have a par value of $0.001 per share. There are no shares of preferred stock outstanding at March 31, 2014.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying unaudited condensed consolidated financial statements have been prepared in accordance with U.S. general accepted accounting principles ("U.S. 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 generally accepted accounting principles 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 March 24, 2014 with the SEC.

The results of operations for the three months ended March 31, 2014 are not necessarily indicative of the results to be expected for the year ending December 31, 2014. The condensed balance sheet as of December 31, 2013 has been derived from audited financial statements at that date but does not include all of the information required by U.S. GAAP for complete financial statements.

Reverse Stock Split

In January 2014, the Company's board of directors and its stockholders approved an amendment to the Company's amended and restated certificate of incorporation to effect a reverse split of shares of the Company's common stock on a 1-for-3.1345 basis (the "Reverse Stock Split"). The par values and the authorized shares of the common and convertible preferred stock were not adjusted as a result of the Reverse Stock Split, nor were the outstanding shares of preferred stock. All issued and outstanding common stock and related per share amounts contained in the financial statements have been retroactively adjusted to reflect this Reverse Stock Split for all periods presented. A proportional adjustment to the conversion ratio for each series of convertible preferred stock was also effected in connection with the Reverse Stock Split. The Reverse Stock Split was effected on January 17, 2014.

Use of Estimates

The preparation of condensed financial statements in conformity with U.S. 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 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, convertible preferred stock and related warrants, common stock, 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 and Cash Equivalents

The Company considers all highly liquid investments with original maturities of three months or less from the date of purchase to be cash equivalents. Cash equivalents consist primarily of amounts invested in money market accounts.

Short-Term Investments

All investments have been classified as “available-for-sale” and are carried at estimated fair value as determined based upon quoted market prices or pricing models for similar securities. Management determines the appropriate classification of its investments in debt securities at the time of purchase and reevaluates such designation as of each balance sheet date. Unrealized gains and losses are excluded from earnings and were reported as a component of comprehensive loss. Realized gains and losses and declines in fair value judged to be other than temporary, if any, on available-for-sale securities are included in interest income and other expense, respectively. The cost of securities sold is based on the specific-identification method. Interest on marketable securities is included in interest income.

Deferred Offering Costs

Deferred offering costs, which primarily consist of direct incremental accounting, legal and printing fees relating to the IPO, were initially capitalized. The deferred offering costs of $3.3 million were subsequently offset against IPO proceeds upon the completion of the IPO in February of 2014. As of December 31, 2013, $2.3 million of deferred offering costs were capitalized and included in prepaid and other current assets on the balance sheet.

Concentration of Credit Risk and Other Risks and Uncertainties

Financial instruments that potentially subject the Company to a concentration of credit risk consist of cash, cash equivalents, and marketable securities. The Company’s cash, cash equivalents, and short-term investments are held by financial institutions that management believes are of high credit quality. The Company’s investment policy limits investments to fixed income securities denominated and payable in U.S. dollars such as U.S. government obligations, money market instruments and funds, corporate bonds, and asset-backed securities and places restrictions on maturities and concentrations by type and issuer. Such deposits may, at times, exceed federally insured limits. The Company has not experienced any losses on its deposits of cash and cash equivalents and its accounts are monitored by management to mitigate risk. The Company is exposed to credit risk in the event of default by the financial institutions holding its cash and cash equivalents and corporate bond issuers to the extent recorded in the balance sheets.

Income Taxes

The Company uses the liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on the differences between the financial reporting and the tax bases of assets and liabilities and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. The Company must then assess the likelihood that the resulting deferred tax assets will be realized. A valuation allowance is provided when it is more likely than not that some portion or all of a deferred tax asset will not be realized. Due to the Company’s lack of earnings history, the net deferred tax assets have been fully offset by a valuation allowance.

The Company recognizes benefits of uncertain tax positions if it is more likely than not that such positions will be sustained upon examination based solely on their technical merits, as the largest amount of benefit that is more likely than not to be realized upon the ultimate settlement. The Company’s policy is to recognize interest and penalties related to the underpayment of income taxes as a component of income tax expense or benefit. To date, there have been no interest or penalties charged in relation to the unrecognized tax benefits.

Net Loss per Share Attributable to Common Stockholders

Basic net loss per share attributable to common stockholders is calculated by dividing the net loss attributable to common stockholders by the weighted-average number of shares of common stock outstanding during the period, without consideration for common stock equivalents. The net loss attributable to common stockholders is calculated by adjusting the net loss of the Company for the accretion on the Series A convertible preferred stock and cumulative dividends paid on Series A and B convertible preferred stock. Diluted net loss per share attributable to common stockholders is the same as basic net loss per share attributable to common stockholders, since the effects of potentially dilutive securities are antidilutive.

3. **Fair Value Measurements**

Financial assets and liabilities are recorded at fair value. The carrying amount of certain financial instruments, including cash and cash equivalents, accounts payable and accrued liabilities approximate fair value due to their relatively short maturities. Assets and liabilities recorded at fair value on a recurring basis in the 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 and liabilities remeasured on a recurring basis based on the three-tier fair value hierarchy (in thousands):

	March 31, 2014			
	Level 1	Level 2	Level 3	Total
Financial Assets:				
Money market funds	$ 33,842	$ —	$ —	$ 33,842
Commercial paper	—	5,985	—	5,985
Corporate bonds	—	118,231	—	118,231
U.S. Government securities	—	2,998	—	2,998
Total financial assets	$ 33,842	$ 127,214	$ —	$ 161,056

	December 31, 2013			
	Level 1	Level 2	Level 3	Total
Financial Assets:				
Money market funds	$ 6,847	$ —	$ —	$ 6,847
Commercial paper	—	1,000	—	1,000
Corporate bonds	—	44,950	—	44,950
Total financial assets	$ 6,847	$ 45,950	$ —	$ 52,797
Financial Liabilities:				
Convertible preferred stock warrant liability	$ —	$ —	$ 3,419	$ 3,419
Total financial liabilities	$ —	$ —	$ 3,419	$ 3,419

The convertible preferred stock warrant liability was classified as a Level 3 liability. As of December 31, 2013, the Company determined the estimated fair value of the warrants using an option-pricing method to allocate the equity value of the Company to the warrants based on the Company's capital structure. The equity value was estimated using the back-solve method, whereby the equity value was derived from a recent transaction involving the Company's own securities. The key inputs used to determine value of the warrants was an estimated fair value of the Company's common stock of $12.14 per share, expected volatility of 70%, the expected time to liquidity event of 0.43 years and risk-free interest rate of 0.11%. The significant unobservable input used in the fair value measurement of the convertible preferred stock warrant liability was the equity value of the Company. Generally, increases (decreases) in the equity value of the Company would result in a directionally similar impact to the fair value measurement of the preferred stock warrant liability.

As of January 30, 2014, the Company determined the estimated fair value of the warrants using the Black-Scholes option-pricing model. Inputs used to determine the fair value included the value of the Company's common stock upon closing of the IPO of $21.00, the remaining contractual term of the warrants of 7.0 years, risk-free interest rate of 2.19% and expected volatility of 70%. The preferred stock warrants were converted to common stock warrants upon the completion of the IPO and are no longer subject to remeasurement.

The following table sets forth a summary of the changes in the estimated fair value of the Company's convertible preferred stock warrants, which were measured at fair value on a recurring basis until their conversion to common stock warrants and related reclassification to additional paid-in capital (in thousands):

	Three Months Ended March 31,	
	2014	2013
Fair value, beginning of period	$ 3,419	$ 518
Change in fair value recorded as a loss in other expense, net	3,324	(2)
Reclassification of warrant liability to additional paid-in capital	(6,743)	—
Fair value, end of period	$ —	$ 516

4. Balance Sheet Components

Cash Equivalents and Short-term Investments

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

	March 31, 2014			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Money market funds classified as cash equivalents	$ 33,842	$ —	$ —	$ 33,842
Corporate bonds classified as cash equivalents	17,263	2	(1)	17,264
Commercial Paper classified as short-term investments	5,985	—	—	5,985
Corporate bonds classified as short-term investments	101,017	18	(68)	100,967
U.S Government securities classified as short-term investments	2,995	3	—	2,998
Total	$ 161,102	$ 23	$ (69)	$ 161,056

	December 31, 2013			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Money market funds classified as cash equivalents	$ 6,847	$ —	$ —	$ 6,847
Commercial Paper classified as short-term investments	1,000	—	—	1,000
Corporate bonds classified as short-term investments	44,939	17	(6)	44,950
Total	$ 52,786	$ 17	$ (6)	$ 52,797

At March 31, 2014, the remaining contractual maturities of available-for-sale securities were less than two years. There have been no significant realized gains or losses on available-for-sale securities for the periods presented.

Accrued Liabilities

Accrued liabilities consist of the following (in thousands):

	March 31, 2014	December 31, 2013
Research and clinical trial expenses	$ 1,372	$ 1,886
Payroll and related expenses	1,557	2,360
Other	309	160
Total accrued liabilities	$ 3,238	$ 4,406

5. **License and Research Agreements**

Nobelpharma License Agreement

In September 2010, the Company entered into a collaboration and license agreement with Nobelpharma Co., Ltd. (Nobelpharma). Under the terms of this collaboration and license agreement, each party granted the other party a worldwide exclusive license under certain of that party's intellectual property related to the compound identified as N-acetylneuraminic acid, also known as sialic acid, to develop, manufacture, and commercialize products. Nobelpharma's licensed territory includes Japan and certain other Asian countries, and the Company's licensed territory includes the rest of the world.

Under the collaboration and license agreement, the Company paid Nobelpharma $110,500 (10 million Yen) for the license, which was recorded as research and development expense in 2010, and also issued 76,567 shares of common stock to Nobelpharma with a minimal value. The Company is required to pay Nobelpharma royalties based on net sales upon product sales commencement. In addition, the Company is required to make certain payments to Nobelpharma based upon achievement of certain development and approval milestones. The Company paid $495,000 in development milestone payments from inception through March 31, 2014. The remaining total aggregate payments, if all milestones are achieved by Nobelpharma, would be 200 million Yen (approximately $1.9 million based on the exchange rate at March 31, 2014). The Company will pay a high single digit royalty on net sales in the Company's territory and will receive a mid-single digit royalty on net sales in the Nobelpharma territory, excluding Japan, if such product sales are ever achieved. Net sales, as defined in the collaboration and license agreement, represent the net sales of products whereby the licensed compound is the active ingredient. If the products include other active ingredients, the portion of the net sales allocated to the licensed compound would be used in determining the royalty payments.

Saint Louis University License Agreement

In November 2010, the Company entered into a license agreement with Saint Louis University (SLU). Under the terms of this license agreement, SLU granted the Company an exclusive worldwide license to make, have made, use, import, offer for sale, and sell therapeutics related to SLU's beta-glucuronidase product for use in the treatment of human diseases.

Under the license agreement, the Company paid SLU an up-front fee of $10,000, which was recorded as research and development expense in 2010. The Company will be required to make a milestone payment of $100,000 upon approval of a glucuronidase-based enzyme therapy for treatment of MPS 7. Additionally, upon reaching a certain level of cumulative worldwide sales of the product, the Company will be required to pay to SLU a low single-digit royalty on net sales of the licensed products in any country or region, if such product sales are ever achieved.

AAI Pharma License Agreement

In March 2011, the Company entered into a license agreement with AAI Pharma Services Corp. (AAI Pharma). Under the terms of this license agreement, AAI Pharma granted the Company a fully paid-up, royalty-free, exclusive, perpetual, and irrevocable license to research, develop, make, have made, use, import, offer for sale, and sell products incorporating AAI Pharma's controlled release matrix solid dose oral tablet. Under the license agreement, the Company will pay a mid-single digit percentage of any sublicense revenue received by Ultragenyx related to the sublicense of AAI Pharma technology that had been initially licensed by Ultragenyx.

HIBM Research Group License Agreement

In April 2012, the Company entered into an exclusive license agreement with HIBM Research Group (HRG). Under the terms of this license agreement, HRG granted the Company an exclusive worldwide license to certain intellectual property related to the treatment of HIBM. Under the license agreement, the Company paid HRG an up-front fee of $25,000 which was recorded as research and development expense during the year ended December 31, 2012. The Company may make future payments that aggregate up to $300,000 and that are contingent upon attainment of various development and approval milestones. Additionally, the Company will pay to HRG a royalty of less than 1% of net sales of the licensed products in the licensed territories, if such product sales are ever achieved.

St. Jude Children's Research Hospital License Agreement

In September 2012, the Company entered into a license agreement with St. Jude Children's Research Hospital (St. Jude). Under the terms of this license agreement, St. Jude granted the Company an exclusive license under certain know-how to research, develop, make, use, offer to sell, import, and otherwise commercialize and exploit St. Jude's protective protein, cathepsin, a protein product to treat, prevent, and/or diagnose galactosialidosis and other monogenetic diseases.

Under the license agreement, the Company paid St. Jude an up-front fee of $10,000 which was recorded as research and development expense during the year ended December 31, 2012. Additionally, the Company will pay to St. Jude a royalty of less than 1% on net sales of the licensed products in the licensed territories, if such product sales are ever achieved.

Baylor Research Institute License Agreement

In September 2012, the Company entered into a license agreement with Baylor Research Institute (BRI). Under the terms of this license agreement, BRI exclusively licensed to the Company certain intellectual property related to triheptanoin for North America. Under the license agreement, the Company paid BRI an up-front fee of $250,000 which was recorded as research and development expense during the year ended December 31, 2012. In June 2013, the Company notified BRI that it was exercising its option pursuant to the agreement to license the rights to triheptanoin in all territories outside of the United States, Canada and Mexico and paid the option exercise fee of $750,000.

The Company may make future payments of up to $10.5 million contingent upon attainment of various development milestones and $7.5 million contingent upon attainment of various sales milestones. Additionally, the Company will pay to BRI a mid-single digit royalty on net sales of the licensed product in the licensed territories, if such product sales are ever achieved.

Kyowa Hakko Kirin Collaboration and License Agreement

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

The Company is accounting for the agreement as a collaboration arrangement as defined in ASC 808, *Collaborative Agreements;* accordingly, the Company recognized $710,000 for its share of the costs as research and development expenses for the three months ended March 31, 2014. For the period from April 22, 2010 (Inception) through March 31, 2014, the Company recognized $1,514,000 for its share of the costs as research and development expenses.

6. Convertible Preferred Stock Warrants and Common Stock Warrants

Upon the closing of the Company's IPO, the Convertible Preferred Stock warrants were converted into warrants to purchase common stock.

As of March 31, 2014, outstanding common stock warrants consisted of the following:

Common Stock Warrants:	Number of Warrants	Date Issued	Term	Exercise Price
Common stock	83,167	June 2010	10 years	$ 3.006
Common stock	203,759	February 2011	10 years	3.006
Common stock	66,533	June 2011	10 years	3.006
Total common stock warrants	353,459			

As of December 31, 2013, outstanding preferred stock warrants consisted of the following:

Convertible Preferred Stock Warrants:	Number of Warrants	Date Issued	Term	Exercise Price
Series A	241,803	June 2010	10 years	$ 1.034
Series A	592,417	February 2011	10 years	1.034
Series A	193,442	June 2011	10 years	1.034
Total convertible preferred stock warrants	1,027,662			

The fair value of the warrants was estimated to be $6.7 million and $3.4 million as of January 30, 2014 (pricing date of IPO) and December 31, 2013, respectively.

The Company recorded ($3.3 million), $2,000, and ($6.5 million) to other income (expense) for three months ended March 31, 2014 and 2013 and for the period from April 22, 2010 (Inception) through March 31, 2014, representing the change in fair value of the warrants for the respective period.

7. Convertible Preferred Stock

The holders of the Series A and Series B convertible preferred stock were entitled to receive cumulative dividends at the rate of $0.062 per share per annum, payable in the form of cash. Dividends accrued from day to day, whether or not declared, but were paid only when, as, and if declared by the Board of Directors. During 2012, $2.1 million of dividends were declared and paid to holders of Series A convertible preferred stock in the form of additional Series A convertible preferred stock. Dividends in arrears as of December 31, 2013 were $4.0 million for both series of preferred stock. Upon the closing of the IPO in February 2014, all shares of convertible preferred stock then outstanding automatically converted in 19,598,486 shares of common stock. In connection with the conversion of the convertible preferred stock, all accrued and outstanding dividends in the amount of $4.3 million were paid.

The Company initially recorded the Series A and Series B convertible preferred stock at their issuance price, which represents the carrying value. The Series A convertible preferred stock was redeemable at any time after June 16, 2017 once a written request to redeem such stock was received by the Company from holders of not less than seventy-five percent of the then outstanding Series A convertible preferred stock. As only the passage of time was required for the Series A convertible preferred stock to become redeemable, the difference in the initial carrying value of the Series A convertible preferred stock and their total redemption value was being accreted from the issuance date through the first redemption date of June 16, 2017. The Company recorded accretion of $4.4 million and $1.1 million for the three months ended March 31, 2014 and 2013, respectively. As a result of the conversion of the preferred stock to common stock in connection with the Company's IPO, the Company is no longer accreting the Series A convertible preferred stock to its previously calculated redemption value.

8. Stock-Based Compensation

2011 Equity Incentive Plan

In 2011, the Company adopted the 2011 Equity Incentive Plan (the 2011 Plan). The 2011 Plan provides for the granting of stock-based awards to employees, directors, and consultants under terms and provisions established by the Board of Directors. Under the terms of the 2011 Plan, options may be granted at an exercise price not less than fair market value. For employees holding more than 10% of the voting rights of all classes of stock, the exercise prices for incentive stock options must be at least 110% of fair market of the common stock on the grant date, as determined by the Board of Directors. The terms of options granted under the 2011 Plan may not exceed ten years. Options granted generally vest over a period of four years. Typically, the vesting schedule for option grants to newly hired employees provides that 1/4 of the grant vests upon the first anniversary of the employee's date of hire, with the remainder of the shares vesting monthly thereafter at a rate of 1/48 of the total shares subject to the option. All other employee options typically vest in equal monthly installments over the four-year vesting schedule. In connection with the Company's IPO, no further grants will be made under this plan and all remaining shares available for grant were transferred to the 2014 Incentive Plan.

2014 Incentive Plan

In 2014, the Company adopted the 2014 Incentive Plan (the 2014 Plan), which became effective upon the closing of the Company's IPO in February 2014. The 2014 Plan had 2,250,000 shares of common stock available for future issuance at the time of its inception, which included 655,038 shares available under the 2011 Plan, which were transferred to the 2014 Plan upon adoption. The 2014 Plan provides for automatic annual increases in shares available for grant, beginning on January 1, 2015 through January 1, 2024. The 2014 Plan provides for the granting of stock-based awards to employees, directors, and consultants under similar terms, conditions and provisions as the 2011 Plan.

Founder's Stock

In connection with the Series A preferred stock financing, the Company entered into a stock repurchase agreement with the founder on June 16, 2011, whereby 2,552,241 shares of common stock previously owned by the founder were subject to repurchase by the Company at the original issuance price in the event that the founder's employment is terminated either voluntarily or involuntarily. The repurchase rights lapsed over a period of two years from June 16, 2011. The Company calculated the estimated fair value of these restricted shares at the time the restriction was added to the shares as $1,199,000 and recorded this amount as stock-based compensation ratably over the period that the repurchase rights lapsed. Stock-based compensation expense pertaining to the founder's stock was $0, $149,000, and $1,199,000 for the three months ended March 31, 2014 and 2013 and for the period from April 22, 2010 (Inception) through March 31, 2014, respectively.

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

	Three Months Ended March 31,		Period from April 22, 2010 (Inception) Through March 31,
	2014	2013	2014
Research and development	$ 705	$ 30	$ 1,156
General and administrative	90	161	1,441
Total stock-based compensation	$ 795	$ 191	$ 2,597

9. Defined Contribution Plan

In March 2013, the Company began to sponsor a 401(k) retirement plan, in which substantially all of its full-time employees are eligible to participate. Eligible participants may contribute a percentage of their annual compensation to this plan, subject to statutory limitations. The Company has not provided any contributions to the plan since its inception through March 31, 2014.

10. Commitments and Contingencies

Commitments

The Company has various manufacturing, clinical, research, and other contracts with vendors in the conduct of the normal course of its business. As of March 31, 2014, the Company had a binding obligation for approximately $850,000 with a manufacturing vendor for the production of a drug substance for one of its product candidates. All other significant contracts as of March 31, 2014 were terminable, with varying provisions regarding termination. If a contract with a specific vendor were to be terminated, the Company would only be obligated for the products or services that the Company had received at the time the termination became effective.

Contingencies

While there are no legal proceedings the Company is aware of, the Company may become party to various claims and complaints arising in the ordinary course of business. Management does not believe that any ultimate liability resulting from any such claims will have a material adverse effect on its results of operations, financial position, or liquidity. However, management cannot give any assurance regarding the ultimate outcome of such claims, and their resolution could be material to the Company for any particular period, depending upon the level of income or loss for the period, as well as the Company's balance sheet.

11. Net Loss per Share Attributable to Common Stockholders

The following table sets forth the computation of the basic and diluted net loss per share attributable to common stockholders (in thousands, except share and per share data):

	Three Months Ended March 31,	
	2014	2013
Numerator:		
Net loss	$ (13,630)	$ (6,735)
Accretion and dividends on convertible preferred stock	(4,808)	(1,470)
Net loss attributable to common stockholders	$ (18,438)	$ (8,205)
Denominator:		
Weighted-average common shares outstanding	21,582,435	3,461,161
Less: weighted-average unvested common shares subject to repurchase	—	(567,164)
Weighted-average shares used to compute net loss per share attributable to common stockholders, basic and diluted	21,582,435	2,893,997
Net loss per share attributable to common stockholders, basic and diluted	$ (0.85)	$ (2.84)

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

	Three Months Ended March 31,	
	2014	2013
Convertible preferred stock	—	19,598,486
Stock options to purchase common stock	2,315,345	1,440,154
Common stock subject to repurchase	—	567,164
Warrants to purchase convertible preferred stock (as if converted)	—	353,459
Warrants to purchase common stock	353,459	—
	2,668,804	21,959,263

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

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

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with the accompanying unaudited consolidated financial statements and related notes in Item 1 and with the audited consolidated financial statements and the related notes included in our Annual Report on Form 10-K for the year ended December 31, 2013.

Overview

We are a development-stage biopharmaceutical company focused on the identification, acquisition, development, and commercialization of novel products for the treatment of rare and ultra-rare diseases, with an initial focus on serious, debilitating metabolic genetic diseases. We focus on diseases for which the unmet medical need is high, the biology for treatment is clear, and for which there are no approved therapies. Since our inception in 2010, we have in-licensed potential treatments for five different diseases that are currently in or have completed Phase 1/2 or Phase 2 clinical studies. Our strategy, which is predicated upon time- and cost-efficient drug development, allows us to pursue multiple programs in parallel with the goal of delivering safe and effective therapies to patients with the utmost urgency.

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

Our biologics pipeline includes the following three product candidates:

— KRN23, or UX023, is an antibody targeting fibroblast growth factor 23, or FGF23, intended for the treatment of X-linked hypophosphatemia, or XLH, a rare genetic disease that impairs bone growth. We are developing KRN23 pursuant to our collaboration with Kyowa Hakko Kirin Co., Ltd., or KHK. KHK has completed one Phase 1 study, one Phase 1/2 study, and one longer-term Phase 1/2 study of KRN23 in adults with XLH. We plan to initiate a Phase 2 pediatric study in 2014. We also expect to continue the clinical development of KRN23 in adults with XLH.

— rhGUS, or UX003, is an enzyme replacement therapy we are developing for the treatment of mucopolysaccharidosis 7, or MPS 7, a rare lysosomal storage disease that often leads to multi-system disease, pervasive skeletal disease, and early death. We initiated a Phase 1/2 clinical study in MPS 7 in December 2013.

— rhPPCA, or UX004, is an enzyme replacement therapy in preclinical development for galactosialidosis, a rare lysosomal storage disease that can cause multi-system clinical disease similar to MPS 7 including enlarged liver, joint disease, abnormal bone development, short stature, and early death. We plan to continue preclinical development of rhPPCA during 2014.

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

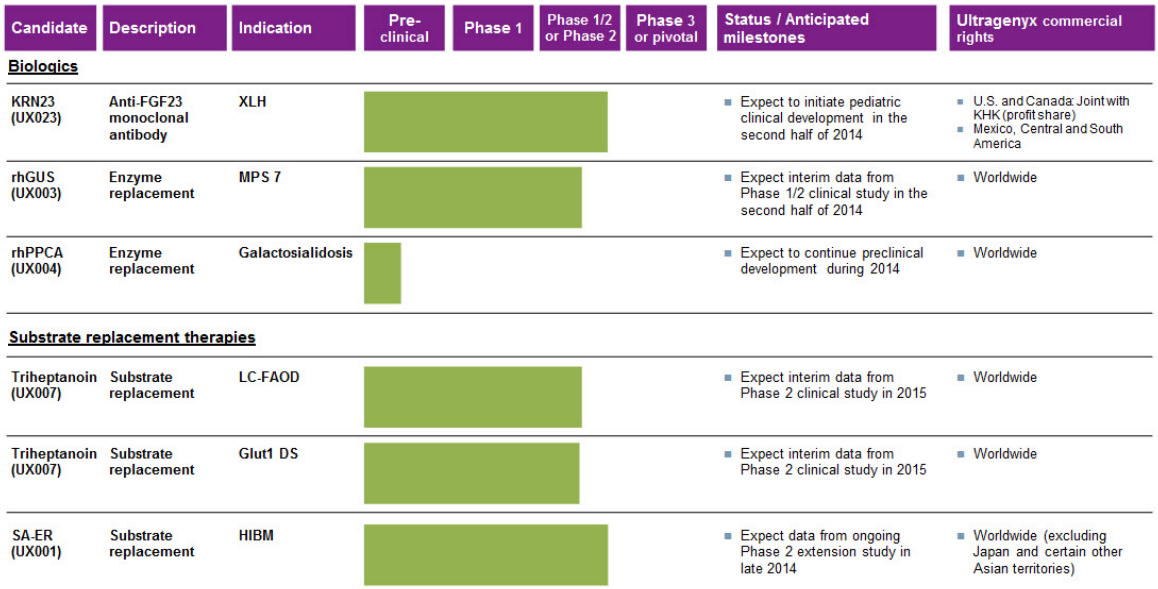
— Triheptanoin, or UX007, is a synthetic triglyceride with a specifically designed chemical composition being studied as an energy substrate replacement therapy in an international open-label Phase 2 study for the treatment of long-chain fatty acid oxidation disorders, or LC-FAOD. This is a set of rare metabolic diseases caused by the inability to convert fat into energy leading to low blood sugar, muscle rupture, and heart and liver disease.

— Triheptanoin is also in a Phase 2 study for the treatment of glucose transporter type-1 deficiency syndrome, or Glut1 DS, a rare metabolic disease of brain energy deficiency that is characterized by seizures, developmental delay, and movement disorder.

— SA-ER, or UX001, is an extended-release form of sialic acid in a Phase 2 extension study for the treatment of hereditary inclusion body myopathy, or HIBM, a neuromuscular disorder that causes muscle weakness and wasting. Data from the Phase 2 study were presented at the American Academy of Neurology (AAN) Annual Meeting in April 2014. We continue to treat the patients from the Phase 2 study in an extension study and anticipate that data from the extension study will be available in late 2014.

Product Candidates

The following table summarizes our current product candidate pipeline:



Candidate	Description	Indication	Pre-clinical	Phase 1	Phase 1/2 or Phase 2	Phase 3 or pivotal	Status / Anticipated milestones	Ultragenyx commercial rights
Biologics								
KRN23 (UX023)	Anti-FGF23 monoclonal antibody	XLH					▪ Expect to initiate pediatric clinical development in the second half of 2014	▪ U.S. and Canada: Joint with KHK (profit share) ▪ Mexico, Central and South America
rhGUS (UX003)	Enzyme replacement	MPS 7					▪ Expect interim data from Phase 1/2 clinical study in the second half of 2014	▪ Worldwide
rhPPCA (UX004)	Enzyme replacement	Galactosialidosis					▪ Expect to continue preclinical development during 2014	▪ Worldwide
Substrate replacement therapies								
Triheptanoin (UX007)	Substrate replacement	LC-FAOD					▪ Expect interim data from Phase 2 clinical study in 2015	▪ Worldwide
Triheptanoin (UX007)	Substrate replacement	Glut1 DS					▪ Expect interim data from Phase 2 clinical study in 2015	▪ Worldwide
SA-ER (UX001)	Substrate replacement	HIBM					▪ Expect data from ongoing Phase 2 extension study in late 2014	▪ Worldwide (excluding Japan and certain other Asian territories)

KRN23 (UX023) for the treatment of XLH

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

In August 2013, we formed a collaboration with KHK to jointly develop and commercialize KRN23 for the treatment of XLH. KHK has conducted one Phase 1 study, one Phase 1/2 study and one longer-term Phase 1/2 study of KRN23 in adults with XLH. We reviewed safety and efficacy data from the Phase 1/2 studies prior to entering into our collaboration with KHK, and we entered into the collaboration based in part upon our conclusion that these data were supportive of further development (serum phosphate, renal tubular reabsorption of phosphate, and vitamin D levels were increased, and the product appeared well tolerated).

Results from the Phase 1 single dose study in 38 adult XLH patients were presented at the American Society for Bone and Mineral Research Annual Meeting in October 2013 and published in the Journal of Clinical Investigation in February 2014. The data demonstrated that KRN23 was well tolerated and increased serum phosphate, or phosphorus, as well as vitamin D levels. Of the 38 adult XLH patients, 12 received a single subcutaneous injection of KRN23 (at doses of 0.1, 0.3, 0.6, or 1.0 mg/kg), 17 received a single intravenous injection of KRN23 (at doses of 0.003, 0.01, 0.03, 0.1, or 0.3 mg/kg) and 9 received placebo. The effect of KRN23 on the increase in serum phosphate levels was comparable between intravenous and subcutaneous administration; however, time to reach peak effect was slower and duration of effect was greater with subcutaneous administration compared with intravenous administration. The demonstrated improvement in serum phosphate levels suggests that significant benefit could be expected. Corresponding changes were observed in renal tubular reabsorption of phosphate. Increases in vitamin D were also observed, suggesting improved intestinal absorption of both phosphate and calcium. Changes were not observed in serum calcium.

No serious adverse events were reported in the Phase 1 study. Approximately 83% of the subjects experienced at least one non-serious treatment-emergent adverse event, the most common of which were nausea and headache; no patients in the placebo or subcutaneous treatment arms reported these events. In the subcutaneous arm, two patients (approximately 17%) experienced elevated levels of the enzyme amylase in the blood, and two other patients (approximately 17%) experienced back pain. There did not appear to be a relationship between the incidence and types of adverse events and the dose administered following a single dose of study drug.

We expect KHK to release data from the completed Phase 1/2 adult repeat-dose studies during 2014.

We plan to initiate a Phase 2 pediatric study in 2014, in patients with radiographic evidence of bone disease, following discussions with multiple regulatory agencies on our pediatric study design. Depending on the results of our Phase 2 pediatric study, we intend to conduct a Phase 3 pediatric trial. Given the high turnover and growth of bone during childhood and the critical role phosphate plays in bone growth, pediatric XLH patients have the highest morbidity and potential for benefit in a shorter timeframe. As a result, pediatric XLH patients may also have the greatest potential for improvement based on third-party data regarding enzyme replacement therapy in hypophosphatasia, which is another genetic bone disease with poor bone mineralization related to phosphate metabolism caused by a different, unrelated mechanism. We also expect to continue to develop KRN23 in adults with XLH and plan to conduct an adult Phase 2b study in parallel with our Phase 3 pediatric trial.

rhGUS (UX003) for the treatment of MPS 7

Recombinant human beta-glucuronidase, or rhGUS, is an intravenous, or IV, enzyme replacement therapy for the treatment of MPS 7, also known as Sly Syndrome. Patients with MPS 7 suffer from severe cellular and organ dysfunction that typically leads to death in the teens or early adulthood. MPS 7 is caused by a deficiency of the lysosomal enzyme beta-glucuronidase, which is required for the breakdown of certain complex carbohydrates known as glycosaminoglycans, or GAGs. The inability to properly break down GAGs leads to their accumulation in many tissues, resulting in a serious multi-system disease. There are currently no approved drug therapies for MPS 7.

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

In December 2013 we initiated an open-label, Phase 1/2 study in the United Kingdom to evaluate the safety, tolerability, efficacy, and dose of IV administration every other week of rhGUS in up to five patients with MPS 7 who are between five and 30 years of age. The initial 12-week treatment period will be followed by a dose-titration period and a long-term extension study. We expect to release interim data from this study during 2014.

Preliminary data from the Phase 1/2 study were presented at the American College of Medical Genetics and Genomics (ACMG) Annual Clinical Genetics Meeting in March 2014. Results from three patients who had been administered 2 mg/kg of rhGUS every other week for two, six, and 12 weeks showed evidence of clearance of lysosomal storage as indicated by the decrease in urinary GAG excretion beginning at two weeks of treatment of approximately 30-50%. At the 12 week assessment of the first patient, absolute liver size was reduced by approximately 11%. This represents a 46% decrease in the excess liver size above normal for age and gender. The remaining patients have not yet reached the 12 week time point for liver size assessment. No serious adverse events were observed during up to 12 weeks of treatment, and no infusion-associated reactions were observed after a total of 13 infusions to date in these three subjects. The Phase 1/2 study will continue, and additional 12-week interim data are expected in the second half of 2014. If these results are supportive, we plan to initiate a pivotal Phase 3 study.

We are also supplying rhGUS to an investigator who is treating a single U.S. patient under an emergency investigational new drug, or eIND, application. Results from the treatment of this patient were presented at the Lysosomal Disease Network's 10th Annual World Symposium in February 2014. Preliminary data showed a reduction in lysosomal storage based on reduced excretion of urinary GAG and a reduction in the size of the enlarged liver and spleen. The patient showed an improvement of pulmonary function and no infusion-associated reactions during the first 14 weeks of treatment. The patient's caregivers also reported improved stamina and increased time spent in school.

The European Medicines Agency, or EMA, has agreed that approval under exceptional circumstances could be possible for a proposed 12-patient placebo-controlled pivotal study in this disease with urinary GAG levels as a surrogate primary endpoint provided the data was strongly supportive of a favorable benefit/risk ratio. The EMA requested that some evidence or trend in improvement in clinical endpoints be observed to support the primary endpoint, but recognized that a statistically significant result on clinical endpoints was unlikely given the small number of patients expected to be enrolled in the study. The United States Food and Drug Administration, or FDA, has not yet agreed to the pivotal study plan and would like to see additional data correlating urinary GAG levels with other clinical endpoints, which we are collecting.

In addition to the above development plan, we intend to study MPS 7 patients under the age of five years, including potentially younger infants born with hydrops fetalis. Currently, these infants often die within a few months to one year, but enzyme replacement therapy might be able to reduce GAG storage and improve health and survival in these patients. This program would not start until we had obtained sufficient information from the Phase1/2 study to support the initiation of a trial in younger patients.

rhPPCA (UX004) for the treatment of galactosialidosis

Recombinant human protective protein cathepsin-A, or rhPPCA, which we in-licensed from St. Jude Children's Research Hospital in September 2012, is in preclinical development as an enzyme replacement therapy for galactosialidosis, a rare lysosomal storage disease for which there are no currently approved drug therapies. Similar to MPS patients, patients with galactosialidosis present with both soft tissue storage in the liver, spleen, and other tissues, as well as connective tissue (bone and cartilage) related disease. As with MPS 7, an enzyme deficiency results in accumulation of substrates in the lysosomes, causing skeletal and organ dysfunction, and death. We plan to continue preclinical development of rhPPCA during 2014.

Triheptanoin (UX007) for the treatment of LC-FAOD

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

We licensed certain intellectual property rights relating to triheptanoin from Baylor Research Institute in August 2012. Triheptanoin has been studied clinically for 13 years in approximately 130 human subjects affected by a variety of diseases, including greater than 60 patients with LC-FAOD. Multiple investigator-sponsored open-label studies suggest clinical improvements with triheptanoin treatment, even for patients who were on standard of care. We recently presented a retrospective medical record review study assessing the clinical outcome of triheptanoin treatment on LC-FAOD subjects who have been participating in a compassionate use program at the University of Pittsburgh Medical Center. The data showed that treatment with triheptanoin appeared to reduce the frequency and severity of hospitalizations previously experienced by these patients for disease-related causes, including muscle rupture, hypoglycemia, and cardiomyopathy. A reduction in mean total hospital days per year from 17.55 to 5.40 (69%; $p = 0.0242$) was observed after transitioning from standard of care to triheptanoin therapy.

Triheptanoin is currently being evaluated in a prospective international open-label Phase 2 study in approximately 30 severely affected LC-FAOD patients. A principal goal of the study is to determine the appropriate clinical endpoints and patient population for testing in potential later-stage pivotal studies. The study will evaluate patients, ages 6 months to 35 years, exhibiting significant clinical manifestations of LC-FAOD despite current therapy. Prior to initiating treatment with triheptanoin, subjects will continue current therapy for four weeks to establish their baseline condition. Triheptanoin will then be titrated to an expected target dose of 25-35% of total daily caloric intake via oral administration, while ensuring tolerability. The study will assess the impact of triheptanoin on several endpoints, including cycle ergometer performance, 12-minute walk test, muscle strength, creatine kinase levels, hypoglycemia, liver size, cardiac disease, and major medical events. The patients will be followed to evaluate the effects of triheptanoin treatment on acute clinical pathophysiology associated with LC-FAOD over 24 weeks, then may continue treatment for an additional 54 weeks for observation of major medical events. Data from this study should be available in 2015.

Triheptanoin (UX007) for the treatment of Glut1 DS

We are also developing triheptanoin for patients with Glut1 DS. Glut1 DS is caused by a mutation affecting the gene that codes for Glut1, which is a protein that transports glucose from the blood into the brain. Because glucose is the primary source of energy for the brain, Glut1 DS results in a chronic state of brain energy deficiency and is characterized by seizures, developmental delay, and movement disorder. There are currently no approved drugs specific to Glut1 DS. The current standard of care for Glut1 DS is the ketogenic diet, an extreme high-fat (70-80% of daily calories as fat)/low-carbohydrate diet, which generates ketone bodies as an alternative energy source to glucose, and one or more antiepileptic drugs. The ketogenic diet can be effective in reducing seizures but compliance can be difficult, and the diet has demonstrated limited effectiveness in the treatment of developmental delay and movement disorders. In addition, ketogenic diet can lead to side effects including renal stones. In general, Glut 1 DS patients are considered relatively refractory to antiepileptic drugs with only approximately 10% achieving seizure control on antiepileptic drugs alone. There are currently no antiepileptic drugs approved specifically for patients with Glut 1 DS.

Triheptanoin is intended as a substrate replacement therapy to provide an alternative source of energy to the brain in Glut1 DS patients. Although an open-label investigator-sponsored clinical study is ongoing and the results have not yet been reported, there are anecdotal reports of benefit in terms of reduced seizures and improved development rate in some Glut1 DS subjects taking triheptanoin. In March 2014, we initiated a Phase 2 global, randomized, double-blind, placebo-controlled, parallel-group study of up to 50 patients who are currently not fully compliant with ketogenic diet and continue to have seizures. The primary efficacy objective is the reduction in frequency of seizures compared to placebo following a 6-week baseline period and subsequent 8-week placebo-controlled treatment period. The blinded treatment period will be followed by an open-label extension period in which patients will be treated with triheptanoin through week 52. Patient enrollment may be modified based on an interim analysis. We expect to release data from this trial in 2015.

We also continue to support investigator-sponsored trials studying triheptanoin across multiple indications.

SA-ER (UX001) for the treatment of HIBM

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

SA-ER is intended as a substrate replacement therapy designed to address sialic acid deficiency and restore muscle function in HIBM patients. We have conducted a Phase 2 randomized, double-blind, placebo-controlled study of SA-ER in 47 HIBM patients. Data from this study were presented at the American Academy of Neurology (AAN) Annual Meeting in April 2014.Patients in the study were initially randomized to receive placebo, 3 grams, or 6 grams of SA-ER per day. After 24 weeks, placebo patients crossed over to either 3 grams or 6 grams total daily dose, on a blinded basis, for an additional 24 weeks. The final analysis compared change at week 48 from baseline for the combined groups at 6 grams versus 3 grams of SA-ER. Assessments included pharmacokinetics, composites of upper extremity and lower extremity muscle strength as measured by dynamometry, other clinical endpoints, patient reported outcomes, and safety.

At 24 weeks, assessments of upper extremity composite of muscle strength showed a statistically significant difference in the 6 gram group compared to placebo (+2.33 kg; 5.5% relative difference from baseline; p=0.040). At 48 weeks, a statistically significant difference between the combined 6 gram group and the combined 3 gram group was observed (+3.44 kg; 8.5% relative difference from baseline; p=0.0033). Patients with less advanced disease (able to walk more than 200 meters at baseline), a predefined subset, showed a more pronounced difference (+4.69 kg; 9.7% relative difference from baseline; p=0.00055). The lower extremity composite showed a similar pattern of response but did not show a statistically significant difference between the dose groups. None of the groups showed a significant decline in the lower extremity composite during the treatment period. A positive trend was seen in patient-reported outcomes of functional activity. SA-ER appeared to be well tolerated with no serious adverse events observed to date in either dose group, and no dose-dependent treatment-emergent adverse events were identified. Most adverse events were mild to moderate and most commonly gastrointestinal and pain related to bone biopsy procedures.

We continue to treat these patients in an extension study evaluating an increased daily dosage of sialic acid based on the dose dependence observed at weeks 24 and 48. We anticipate that data from the extension study should be available in late 2014. We also plan to discuss data from this program with regulatory authorities during 2014.

Financial Operations Overview

We are considered a development-stage company under U.S. generally accepted accounting principles, or U.S. GAAP, and have only a limited operating history. To date, we have invested substantially all of our efforts and financial resources to identifying, acquiring, and developing our product candidates, including conducting clinical studies and providing general and administrative support for these operations. To date, we have funded our operations primarily from the sale of convertible preferred stock and equity securities.

We have never been profitable and have incurred net losses in each year since inception. Our net losses were $13.6 million and $6.7 million for the three months ended March 31, 2014 and 2013. As of March 31, 2014 we had incurred cumulative net losses of $73.2 million. Substantially all of our net losses have resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations.

Revenue

To date, we have not generated any revenue. We do not expect to receive revenue from any product candidates that we develop unless regulatory approvals are obtained for our products or we enter into collaborative agreements with third parties.

Research and Development Expenses

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

- expenses incurred under agreements with clinical study sites that conduct research and development activities on our behalf;
- expenses incurred under license agreements with third parties;
- employee and consultant-related expenses, which include salaries, benefits, travel, and stock-based compensation;
- laboratory and vendor expenses related to the execution of preclinical, non-clinical, and clinical studies;

- the cost of acquiring, developing, and manufacturing clinical study materials; and
- facilities, depreciation, and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance, and other supply costs.

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

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

General and Administrative Expenses

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

Interest income

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

Other expense, net

Other expense, net primarily consists of gains and losses resulting from the remeasurement of our convertible preferred stock warrant liability. We recorded adjustments to the estimated fair value of the convertible preferred stock warrants until their conversion into warrants to purchase shares of our common stock at the completion of our initial public offering. At that time, we reclassified the convertible preferred stock warrant liability to additional paid-in capital which will no longer be subject to fair value adjustments.

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 financial statements, which have been prepared in accordance with U.S. GAAP. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. There have been no significant and material changes in our critical accounting policies during the three months ended March 31, 2014, as compared to those disclosed in "Management's Discussion and Analysis of Financial Condition and Results of Operations-Critical Accounting Policies and Significant Judgments and Estimates" in our in our most recent Annual Report on Form 10-K filed with the SEC.

Results of Operations

Comparison of the three months ended March 31, 2014 and 2013:

Research and Development Expenses (dollars in thousands)

	Three Months Ended March 31, 2014	2013	Dollar Change	% Change
Development candidate:				
KRN23	$ 877	$ —	$ 877	*
rhGUS	1,329	2,142	(813)	-38%
rhPPCA	110	71	39	55%
Triheptanoin (LC-FAOD)	1,382	866	516	60%
Triheptanoin (Glut 1 DS)	1,026	42	984	2343%
SA-ER	2,246	1,832	414	23%
Other research and development costs	1,383	711	672	95%
Total research and development expenses	$ 8,353	$ 5,664	$ 2,689	47%

**not meaningful*

Research and development expenses increased $2.7 million for the three months ended March 31, 2014 compared to the same period in 2013. The increase in research and development expenses above is primarily due to:

- for KRN23, an increase of $0.9 million related to development of our pediatric trial design, other development planning, and regulatory activities, since the product candidate was in-licensed in August 2013;
- for rhGUS, a decrease of $0.8 million due to a reduced level of process development and manufacturing activity, partially offset by an increase in clinical trial activities;
- for triheptanoin (LC-FAOD), an increase of $0.5 million related to the initiation of our clinical program, support of investigator-sponsored trials, and costs related to manufacturing;
- for triheptanoin (Glut1 DS), an increase of $1.0 million related to the initiation of our clinical program, and drug production, since the product candidate was in-licensed in August 2013;
- for SA-ER, an increase of $0.4 million related to the increase in clinical and manufacturing activities for this program; and
- an increase of $0.7 million in other research and development costs in support of our product candidate pipeline.

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

General and Administrative Expenses (dollars in thousands)

	Three Months Ended March 31, 2014	2013	Dollar Change	% Change
General and administrative	$ 1,986	$ 1,083	$ 903	83%

General and administrative expenses increased $0.9 million for the three months ended March 31, 2014 compared to the same period in 2013. The increase in general and administrative expenses was primarily due to increases in professional services costs and in personnel costs resulting from an increase in employees in support of our activities.

We expect general and administrative expenses to increase in order for us to continue to support the costs of being a public company.

Interest Income (dollars in thousands)

	Three Months Ended March 31, 2014	2013	Dollar Change	% Change
Interest income	$ 93	$ 26	$ 67	258%

Interest income increased $0.1 million for the three months ended March 31, 2014 compared to the same period in 2013, primarily due to funds invested in 2014 from the closing of our IPO in February 2014.

Other Expense, net (dollars in thousands)

	Three Months Ended March 31, 2014	2013	Dollar Change	% Change
Other expense, net	$ 3,384	$ 14	$ 3,370	24071%

Other expense, net increased $3.4 million for the three months ended March 31, 2014 compared to the same period in 2013. This was primarily due to the $3.3 million increase in expense for the fair value remeasurement of the liability related to our convertible preferred stock warrants. The preferred stock warrants were converted to common stock warrants upon the completion of the IPO and are no longer subject to remeasurement.

Liquidity and Capital Resources

Since our inception, we have funded our operations primarily with $103.9 million in net proceeds from the sale of convertible preferred stock and $121.7 million in net proceeds from the sale of common stock in our IPO. As of March 31, 2014, we had $165.4 million in available cash, cash equivalents, and short-term investments and a deficit accumulated during the development stage of $73.2 million. Our cash, cash equivalents and investments are held in a variety of interest-bearing accounts, including corporate debt securities and money market accounts. Cash in excess of immediate requirements is invested with a view toward liquidity and capital preservation, and we seek to minimize the potential effects of concentration and credit risk.

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

	Three Months Ended March 31, 2014	2013
Cash used in operating activities	$ (8,336)	$ (6,293)
Cash used in investing activities	(65,398)	(15,100)
Cash provided by financing activities	121,754	1
Net increase (decrease) in cash and cash equivalents	$ 48,020	$ (21,392)

Cash Used in Operating Activities

Our primary use of cash is to fund operating expenses, which consist primarily of research and development expenditures. Due to our significant research and development expenditures, we have generated significant operating losses since our inception. Cash used to fund operating expenses is impacted 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 three months ended March 31, 2014 was $8.3 million and reflected a net loss of $13.6 million, offset by non-cash charges of $0.1 million for depreciation and amortization, $0.5 million for the amortization of premium paid on purchased short-term investments, $0.8 million for stock-based compensation and $3.3 million for the revaluation of convertible preferred stock warrant liability. Cash used in operating activities also reflected a $2.4 million increase in prepaid expenses and other current assets primarily due to an increase in contract research organization (CRO) prepaid expenses and an increase in interest income receivable as our invested funds increased with the closing of our IPO in February 2014, a $2.1 million increase in accounts payable primarily due to higher clinical study and related costs, a $2.1 million decrease in other assets primarily related to the reclassification to permanent equity for the deferred offering costs related to our IPO, and a $1.2 million decrease in accrued expenses and other liabilities as a result of a decrease of accrued IPO costs and employee bonuses and an increase in clinical study and related costs as we continued to increase our research and development activities.

Cash used in operating activities for the three months ended March 31, 2013 was $6.3 million and reflected a net loss of $6.7 million, offset by non-cash charges of $0.1 million for depreciation and amortization, $0.2 million for stock-based compensation, and insignificant expenses for the amortization of discounts on purchased short-term investments and the revaluation of the convertible preferred stock warrant liability. Cash used in operating activities reflected an increase in accounts payable and accrued and other liabilities of $1.0 million related to higher clinical study and related costs and other research and development activities and an increase of $0.9 million in prepaid and other current assets related to interest receivable on short-term investments and costs of research and development activities.

Cash Used in Investing Activities

Cash used in investing activities for the three months ended March 31, 2014 was $65.4 million and related to purchases of short-term investments of $88.0 million and property and equipment of $0.6 million and an increase of $0.3 million in restricted cash for the expansion of the space under our current lease, offset by proceeds from maturities of short-term investments of $23.5 million.

Cash used in investing activities for the three months ended March 31, 2013 was $15.1 million and related to purchases of property and equipment of $0.2 million and purchases of short-term investments of $14.9 million.

Cash Flows Provided by Financing Activities

Cash provided by financing activities for the three months ended March 31, 2014 was $121.8 million and was comprised of $126.1 million in proceeds from the issuance of common stock from our IPO and proceeds from the exercise of stock options, offset by the payment of a $4.3 million dividend to our preferred stockholders in connection with the closing of our IPO.

Cash provided by financing activities for the three months ended March 31, 2013 was insignificant.

Funding Requirements

We believe that our existing capital resources, including net proceeds we received from the closing of our IPO in February 2014, will be sufficient to fund our current operations into 2016. We anticipate that we will continue to generate losses for the foreseeable future, and we expect the losses to increase as we continue the development of, and seek regulatory approvals for, our product candidates, and begin to commercialize any approved products. We expect that we will require additional capital to fund our operations and complete our ongoing and planned clinical studies, and funding may not be available to us on acceptable terms or at all. We expect to finance future cash needs through equity or debt financings, strategic collaborations, or grants. 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, or terminate our product development or 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 sales, marketing, and distribution capabilities; and
- the terms and timing of any collaborative, licensing, and other arrangements that we may establish, including any required milestone and royalty payments thereunder.

If we need to raise additional capital to fund our operations, funding may not be available to us on acceptable terms or at all. If we are unable to obtain adequate financing when needed, we may have to delay, reduce the scope of or suspend one or more of our clinical studies, research and development programs or commercialization efforts. We may seek to raise any necessary additional capital through a combination of public or private equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements and other marketing and distribution arrangements. To the extent that we raise additional capital through marketing and distribution arrangements or other collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our product candidates, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. If we do raise additional capital through public or private equity offerings, the ownership interest of our existing stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights. If we raise additional capital through debt financing, we may be subject to covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

Contractual Obligations

The following table summarizes our significant binding contractual obligations at March 31, 2014 (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	$ 586	$ 1,340	$ 1,421	$ 60	$ 3,407
Manufacturing contract	850	—	—	—	850
Total	$ 1,436	$ 1,340	$ 1,421	$ 60	$ 4,257

Off-Balance Sheet Arrangements

Since our inception, 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***

QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Our exposure to market risk for changes in interest rates relates primarily to interest earned on our cash equivalents and marketable securities. 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 March 31, 2014, we had cash, cash equivalents, and short-term investments totaling $165.4 million consisting of bank deposits, money market funds, and investment-grade corporate bonds which are subject to default, changes in credit rating, and changes in market value. The securities in our investment portfolio are classified as available for sale and are subject to interest rate risk and will decrease in value if market interest rates increase. A hypothetical 10% change in interest rates during any of the period presented would not have had a material impact on our financial statements. To date, we have not experienced a loss of principal on any of our investments.

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

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

Evaluation of Disclosure Controls and Procedures

We carried out an evaluation, under the supervision and with the participation of our management, including our Chief Executive Officer and our Chief Financial Officer, of the effectiveness of our “disclosure controls and procedures” as of the end of the period covered by this report, pursuant to Rules 13a-15(b) and 15d-15(b) under the Securities Exchange Act of 1934, as amended, or the Exchange Act. In connection with that evaluation, our Chief Executive Officer and our Chief Financial Officer concluded that our disclosure controls and procedures were effective 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 March 31, 2014. 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 has been no change in our internal control over financial reporting (as defined in Rule 13a-15(f) under the Exchange Act) during our first fiscal quarter ended March 31, 2014, 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.

Item 1A. *Risk Factors*

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

Risks Related to Our Financial Condition and Capital Requirements

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

We are a development-stage biopharmaceutical company with a limited operating history. We have incurred net losses in each year since our inception in April 2010, including net losses of $13.6 million and $6.7 million for the three months ended March 31, 2014 and 2013, respectively. As of March 31, 2014, we had incurred cumulative net losses of $73.2 million.

We have devoted substantially all of our financial resources to identifying, acquiring, and developing our product candidates, including conducting clinical studies, developing manufacturing processes, and providing general and administrative support for these operations. To date, we have financed our operations primarily through the sale of equity securities. The amount of our future net losses will depend, in part, on the rate of our future expenditures and our ability to obtain funding through equity or debt financings, strategic collaborations, or grants. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We are in the early stages of clinical development for our product candidates, we have not yet commenced pivotal clinical studies for any product candidate and it may be several years, if ever, before we complete pivotal clinical studies and have a product candidate approved for commercialization. If we obtain regulatory approval to market a product candidate, our future revenue will depend upon the size of any markets in which our product candidates may receive approval, and our ability to achieve sufficient market acceptance, pricing, reimbursement from third-party payors, and adequate market share for our product candidates in those markets. However, even if we obtain adequate market share for our product candidates, because the potential markets in which our product candidates may ultimately receive regulatory approval are very small, and our expenses may be greater than expected, we may never become profitable despite obtaining such market share and acceptance of our products.

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

- continue our research and nonclinical and clinical development of our product candidates;
- expand the scope of our current clinical studies for our product candidates;
- advance our programs into more expensive clinical studies;
- initiate additional nonclinical, clinical, or other studies for our product candidates;
- pursue preclinical and clinical development for additional indications for existing product candidates;
- change or add additional manufacturers or suppliers;
- seek regulatory and marketing approvals for our product candidates that successfully complete clinical studies;
- establish a sales, marketing, and distribution infrastructure to commercialize any products for which we may obtain marketing approval;
- seek to identify, assess, acquire, and/or develop other product candidates;
- make milestone or other payments under any license agreements;
- seek to maintain, protect, and expand our intellectual property portfolio;
- seek to attract and retain skilled personnel;
- create additional infrastructure to support our operations as a public company and our product development and planned future commercialization efforts; and
- experience any delays or encounter issues with any of the above, including but not limited to failed studies, complex results, safety issues, or other regulatory challenges that require longer follow-up of existing studies, additional major studies, or additional supportive studies in order to pursue marketing approval.

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

We have never generated any revenue from product sales and may never be profitable.

We have no products approved for commercialization and have never generated any revenue. Our ability to generate revenue and achieve profitability depends on our ability, alone or with strategic collaboration partners, to successfully complete the development of, and obtain the regulatory and marketing approvals necessary to commercialize one or more of our product candidates. We do not anticipate generating revenue from product sales in the near future. Our ability to generate future revenue from product sales depends heavily on our success in many areas, including but not limited to:

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

Even if one or more of the product candidates that we develop is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. Our expenses could increase beyond expectations if we are required by the U.S. Food and Drug Administration, or the FDA, the European Medicines Agency, or the EMA, or other regulatory agencies, domestic or foreign, to change our manufacturing processes or assays, or to perform clinical, nonclinical, or other types of studies in addition to those that we currently anticipate. In cases where we are successful in obtaining regulatory approvals to market one or more of our product candidates, our revenue will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval, the accepted price for the product, the ability to get reimbursement at any price, and whether we own the commercial rights for that territory. If the number of our addressable rare disease patients is not as significant as we estimate, the indication approved by regulatory authorities is narrower than we expect, or the reasonably accepted population for treatment is narrowed by competition, physician choice or treatment guidelines, we may not generate significant revenue from sales of such products, even if approved. For example, the development of KRN23, rhGUS, and triheptanoin for pediatric use is an important part of our current business strategy; if we are unable to obtain regulatory approval for the desired age ranges, our business may suffer. Additionally, if we are not able to generate revenue from the sale of any approved products, we may never become profitable.

We expect that we will need to raise additional funding before we can expect to become profitable from sales of our products. This additional financing may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed may force us to delay, limit, or terminate our product development efforts or other operations.

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

As of March 31, 2014, our available cash, cash equivalents and short-term investments were $165.4 million. We expect that our existing cash, cash equivalents and short-term investments, including $121.7 million in net proceeds we received from the closing of our initial public offering, or IPO, in February 2014, will be sufficient to fund our current operations into 2016; however, we expect that we will require additional capital to obtain regulatory approval for, and to commercialize, our product candidates. In addition, our operating plans may change as a result of many factors that may currently be unknown to us, and we may need to seek additional funds sooner than planned. Our future funding requirements will depend on many factors, including but not limited to:

- the scope, rate of progress, results and cost of our clinical studies, nonclinical testing, and other related activities;

- the cost of manufacturing clinical supplies, and establishing commercial supplies, of our product candidates and any products that we may develop;
- the number and characteristics of product candidates that we pursue;
- the cost, timing, and outcomes of regulatory approvals;
- the cost and timing of establishing sales, marketing, and distribution capabilities; and
- the terms and timing of any collaborative, licensing, and other arrangements that we may establish, including any required milestone and royalty payments thereunder.

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

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

Risks Related to the Discovery and Development of Our Product Candidates

We are heavily dependent on the success of our product candidates, which are in the early stages of clinical development. We cannot give any assurance that any of our product candidates will receive regulatory approval, which is necessary before they can be commercialized.

To date, we have invested substantially all of our efforts and financial resources to identifying, acquiring, and developing our product candidates, including conducting clinical studies and providing general and administrative support for these operations. Our future success is dependent on our ability to successfully develop, obtain regulatory approval for, and then successfully commercialize one or more product candidates. We currently generate no revenue from sales of any drugs, and we may never be able to develop or commercialize a marketable drug.

Each of our product candidates is in the early stages of development and will require additional clinical development, management of nonclinical, clinical, and manufacturing activities, regulatory approval, obtaining adequate manufacturing supply, building of a commercial organization, and significant marketing efforts before we generate any revenue from product sales. We currently have five programs that are currently in or have completed Phase 1/2 or Phase 2 clinical studies. None of our product candidates have advanced into a pivotal study and it may be years before such study is initiated, if at all. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from the FDA or comparable foreign regulatory authorities, and we may never receive such regulatory approval for any of our product candidates.

Although certain of our employees have prior experience with submitting marketing applications to the FDA or comparable foreign regulatory authorities, we as a company have not submitted such applications for our product candidates. We cannot be certain that any of our product candidates will be successful in clinical studies or receive regulatory approval. Further, our product candidates may not receive regulatory approval even if they are successful in clinical studies. If we do not receive regulatory approvals for our product candidates, we may not be able to continue our operations.

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

The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time consuming, and inherently unpredictable. If we are ultimately unable to obtain regulatory approval for our product candidates, our business will be substantially harmed.

The time required to obtain approval by the FDA and comparable foreign authorities is unpredictable, typically takes many years following the commencement of clinical studies, and depends upon numerous factors. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions, which may cause delays in the approval or the decision not to approve an application. We have not obtained regulatory approval for any product candidate, and it is possible that none of our existing product candidates or any product candidates we may seek to develop in the future will ever obtain regulatory approval.

Applications for our product candidates could fail to receive regulatory approval for many reasons, including but not limited to the following:

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

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

Clinical drug development involves a lengthy and expensive process with an uncertain outcome, and results of earlier studies may not be predictive of future study results.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical study process. The results of nonclinical studies and early clinical studies of our product candidates may not be predictive of the results of later-stage clinical studies. Product candidates that have shown promising results in early-stage clinical studies may still suffer significant setbacks in subsequent clinical studies. For example, the safety or efficacy results generated to date in clinical studies for KRN23, rhGUS, triheptanoin, and SA-ER do not ensure that later clinical studies will demonstrate similar results. Results from investigator sponsored trials or compassionate use studies may negatively impact the prospects for our programs. 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. Moreover, nonclinical and clinical data are often susceptible to varying interpretations and analyses. We do not know whether any clinical studies we may conduct will demonstrate consistent or adequate efficacy and safety sufficient to obtain regulatory approval to market our drug candidates.

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

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

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

- we estimate that several thousand patients in the United States suffer from XLH, for which KRN23 is being studied;
- we estimate that up to approximately 200 patients in the developed world may suffer from MPS 7, for which rhGUS is being studied;
- we estimate that several thousand patients in the United States suffer from LC-FAOD, for which triheptanoin is being studied;
- we estimate that several thousand patients in the United States suffer from Glut1 DS, for which triheptanoin is being studied; and
- we estimate that about 1,200 to 2,000 patients in the developed world suffer from HIBM, for which SA-ER is being studied.

In addition to the rarity of these diseases, the eligibility criteria of our clinical studies will further limit the pool of available study participants as we will require that patients have specific characteristics that we can measure or to assure their disease is either severe enough or not too advanced to include them in a study. Additionally, the process of finding and diagnosing patients may prove costly. We also may not be able to identify, recruit, and enroll a sufficient number of patients to complete our clinical studies because of the perceived risks and benefits of the product candidate under study, the availability and efficacy of competing therapies and clinical studies, the proximity and availability of clinical study sites for prospective patients, and the patient referral practices of physicians. 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.

If we experience delays in the completion of, or termination of, any clinical study of our product candidates, the commercial prospects of our product candidates will be harmed, and our ability to generate product revenue from any of these product candidates could be delayed or prevented. In addition, any delays in completing our clinical studies will increase our costs, slow down our product candidate development and approval process, and jeopardize our ability to commence product sales and generate revenue. Any of these occurrences may harm our business, financial condition, and prospects significantly. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical studies may also ultimately lead to the denial of regulatory approval of our product candidates.

We may encounter substantial delays in our clinical studies, or we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities.

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

- inability to generate sufficient preclinical, toxicology, or other *in vivo* or *in vitro* data to support the initiation or continuation of human clinical studies or filings for regulatory approval;
- delays in reaching a consensus with regulatory agencies on study design;
- delays in reaching agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical study sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical study sites;
- delays in obtaining required Institutional Review Board, or IRB, approval at each clinical study site;
- changes in clinical study design or development strategy resulting in delays related to obtaining approvals from IRBs and/or regulatory agencies to proceed with clinical studies;
- failure to gain approval from competent authorities or IRBs to conduct clinical studies in certain countries;

- imposition of a clinical hold by regulatory agencies due to a safety concern, after review of an investigational new drug, or IND, application or amendment, or equivalent application or amendment, or an inspection of our clinical study operations or study sites;
- delays in recruiting suitable patients to participate in our clinical studies;
- difficulty collaborating with patient groups and investigators;
- failure by our CROs, other third parties, or us to adhere to clinical study requirements;
- failure to perform in accordance with the FDA's good clinical practices requirements, or applicable regulatory guidelines in other countries;
- delays in having patients complete participation in a study or return for post-treatment follow-up;
- patients dropping out of a study;
- occurrence of adverse events associated with the product candidate that are viewed to outweigh its potential benefits;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;
- the cost of clinical studies of our drug candidates being greater than we anticipate;
- clinical studies of our drug candidates producing negative or inconclusive results, which may result in us deciding, or regulators requiring us, to conduct additional clinical or nonclinical studies or abandon drug development programs;
- competing clinical studies of potential alternative product candidates or investigator-sponsored trials 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 impair our ability to generate revenue. In addition, if we make manufacturing or formulation changes to our product candidates, such as our plan to manufacture a combination extended release and immediate release version of sialic acid, or new formulations of triheptanoin, we may need to conduct additional studies to bridge our modified product candidates to earlier versions. Clinical study delays could also shorten any periods during which our products have patent protection and may allow our competitors to bring products to market before we do, which could impair our ability to obtain orphan exclusivity and to successfully commercialize our product candidates and may harm our business and results of operations.

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

Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay, or halt clinical studies or further development, and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign authorities. Our product candidates are in the early stages of development and the safety profile has not been established. In the completed Phase 1 study, patients treated with KRN23 have experienced nausea, headache, elevated serum amylase, and back pain. Most of these adverse events were mild and no serious adverse events have been observed. Only single-dose Phase 1 data for KRN23 has been reported to date and other side effects may result from repeated dosing and/or longer-term exposure. Patients treated with triheptanoin have experienced drug-related side effects such as cramping, diarrhea, and loose stools. In addition, during a 13-year study of approximately 130 human subjects, including greater than 60 with LC-FAOD, three serious adverse events were classified as possibly related to triheptanoin treatment (muscle cell rupture and elevated creatine kinase reported for two subjects and myoglobinuria in one subject); however, these serious adverse events can be considered typical of the underlying disease. While we have not completed our own clinical studies for triheptanoin, there may be other side effects associated with its use that we discover. Additionally, patients treated with SA-ER have experienced drug-related side effects including mild gastrointestinal discomfort. Enzyme replacement therapies have been associated with infusion-associated reactions due to a developing allergy to the product, which can cause rashes, pain, significant clinical disease, or even death. Our rhGUS and rhPPCA product candidates may also cause these or similar side effects as further development proceeds. Results of our studies 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, the ability of enrolled patients to complete the study, or result in potential product liability claims. We currently carry product liability insurance in the amount of $5.0 million per incident and $5.0 million in the aggregate, and we are required to maintain product liability insurance pursuant to certain of our license 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 successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business. In addition, regardless of merit or eventual outcome, product liability claims may result in impairment of our business reputation, withdrawal of clinical study participants, costs due to related litigation, distraction of management's attention from our primary business, initiation of investigations by regulators, substantial monetary awards to patients or other claimants, the inability to commercialize our product candidates, and decreased demand for our product candidates, if approved for commercial sale.

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

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

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

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

If our product candidates are approved, they will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, 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 current Good Manufacturing Practices, or cGMP, regulations. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any NDA, BLA, marketing authorization application, or 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 to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase IV clinical trials, and surveillance to monitor the safety and efficacy of the product candidate. We will be required to report certain adverse events and manufacturing problems, if any, to the FDA and comparable foreign regulatory authorities. Any new legislation addressing drug safety issues could result in delays in product development or commercialization, or increased costs to assure compliance. We will have to comply with requirements concerning advertising and promotion for our products. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved label. As such, we may not promote our products for indications or uses for which they do not have approval. The holder of an approved NDA, BLA, MAA, or other comparable application, must submit new or supplemental applications and obtain approval for certain changes to the approved product, product labeling, or manufacturing process. We could also be asked to conduct post-marketing clinical studies to verify the safety and efficacy of our products in general or in specific patient subsets. If original marketing approval were obtained via the accelerated approval pathway, we could 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.

If a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, or disagrees with the promotion, marketing or labeling of a product, such regulatory agency may impose restrictions on that product or us, including requiring withdrawal of the product from the market. If we fail to comply with applicable regulatory requirements, a regulatory agency or enforcement authority may, among other things:

- issue warning 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; or
- seize or detain products, or require a product recall.

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.

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 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-party CROs to monitor and manage data for our ongoing nonclinical and clinical programs. We rely on these parties for execution of our nonclinical and clinical studies, and control only certain aspects of their activities. 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 does not relieve us of our regulatory responsibilities. We and our CROs and other vendors are required to comply with cGMP, current good clinical practices, or cGCP, and Good Laboratory Practices, or GLP, which are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area, or EEA, 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 vendors 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 require us to perform additional nonclinical and clinical studies before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical studies comply with cGCP regulations or that nonclinical studies comply with GLP regulations. In addition, our clinical studies must be conducted with product produced under cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical or nonclinical studies, which would delay the regulatory approval process.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs or do so on commercially reasonable terms. In addition, our CROs are not our employees, and except for remedies available to us under our agreements with such CROs, we cannot control whether or not they devote sufficient time and resources to our on-going nonclinical and clinical programs. If CROs 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 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.

Switching or adding additional CROs involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO 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 CROs, 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 prospects.

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

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

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

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

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

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

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

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

- the manufacturing facilities in which our product candidates are made could be adversely affected by equipment failures, labor shortages, raw material shortages, natural disasters, power failures, and numerous other factors.

Although we have not experienced any significant manufacturing problems, any adverse developments affecting manufacturing operations for our product candidates may result in shipment delays, inventory shortages, lot failures, withdrawals or recalls, or other interruptions in the supply of our product candidates. We may also have to take inventory write-offs and incur other charges and expenses for product candidates that fail to meet specifications, undertake costly remediation efforts, or seek more costly manufacturing alternatives.

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

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

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

All entities involved in the preparation of therapeutics for clinical studies or commercial sale, including our existing contract manufacturers for our product candidates, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in clinical studies must be manufactured in accordance with cGMP. These regulations govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of contaminants or to inadvertent changes in the properties or stability of our product candidates that may not be detectable in final product testing. We, our collaborators, or our contract manufacturers must supply all necessary documentation in support of an NDA, BLA, MAA, or other application for regulatory approval, on a timely basis and must adhere to GLP, cGMP, 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 completely dependent on, our contract manufacturing partners for compliance with the regulatory requirements. If these facilities do not pass a pre-approval plant inspection, regulatory approval of the products may not be granted or may be substantially delayed until any violations are corrected to the satisfaction of the regulatory authority, if ever.

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

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

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

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

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

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

Risks Related to Commercialization of Our Product Candidates

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

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

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

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

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

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

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

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

The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. We are currently aware of various existing therapies that may compete with our product candidates. For example, XLH is currently treated with oral phosphate and Vitamin D therapy, which may compete with KRN23. Furthermore, B. Braun Medical Inc., or B. Braun, has received orphan drug designation for triheptanoin in Europe for certain LC-FAOD indications and B. Braun may be evaluating whether or not to initiate clinical development. Triheptanoin is also available and is currently being studied in food-grade form, which may compete with our pharmaceutical-grade product. Investigator-sponsored trials evaluating triheptanoin in multiple indications are ongoing. LC-FAOD is currently treated with diet therapy and medium-chain triglyceride oil, which may compete with triheptanoin. Glut1 DS is currently treated primarily with the ketogenic diet and anti-epileptic drugs, which may also compete with triheptanoin. Additionally, we are aware of a program at the National Institutes of Health, whose intellectual property rights are licensed to a company in New Zealand that is investigating the use of another metabolite in the sialic acid pathway, ManNAc, for the treatment of HIBM, which could compete with SA-ER. ManNAc may have a potential advantage over SA-ER in that it is not a charged molecule like sialic acid is, which might improve its distribution and uptake. Gene therapy, gene correction, RNA-based therapies, and other approaches may also emerge for the treatment of any of the disease areas in which we focus.

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

We currently have no marketing and sales organization. If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our product candidates, we may be unable to generate any revenue.

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

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

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

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

- the efficacy of the product as demonstrated in clinical studies and potential advantages over competing treatments;
- the prevalence and severity of any side effects, including any limitations or warnings contained in a product's approved labeling;
- the clinical indications for which approval is granted;
- relative convenience and ease of administration;
- the cost of treatment, particularly in relation to competing treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the 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 third-party payors on the benefits of the product candidates may require significant resources and may never be successful. If our product candidates are approved but fail to achieve an adequate level of acceptance by physicians, patients, third-party payors, and others in the medical community, we will not be able to generate sufficient revenue to become or remain profitable.

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

Our target patient populations are small, and accordingly the pricing, coverage, and reimbursement of our product candidates, if approved, must be adequate to support our commercial infrastructure. Our per-patient prices must be sufficient to recover our development and manufacturing costs and potentially achieve profitability. Accordingly, the availability and adequacy of coverage and reimbursement by governmental and private payors are essential for most patients to be able to afford expensive treatments such as ours, assuming approval. Sales of our product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be paid for by health maintenance, managed care, pharmacy benefit, and similar healthcare management organizations, or reimbursed by government authorities, private health insurers, and other third-party payors.

If coverage and reimbursement are not available, or are available only to limited levels, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a return on our investment.

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

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

Moreover, increasing efforts by governmental and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for new products approved and, as a result, they may not cover or provide adequate payment for our product candidates. We expect to experience pricing pressures in connection with the sale of any of our product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products.

Risks Related to Our Intellectual Property

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

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

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

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

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

Although we have a number of patents covering methods of use and certain compositions of matter, we do not have complete patent protection for our product candidates. For example, there is no patent coverage for KRN23 in Latin America, where we have rights to commercialize the compound. Therefore, a competitor could develop the same or similar antibody as well as other approaches that target FGF23. Additionally, none of the current intellectual property relating to rhGUS covers composition of matter,

and there are currently no patents that cover rhPPCA. Therefore, it is possible that a competitor could develop the same or similar enzyme with respect to rhGUS and/or rhPPCA, subject to any regulatory exclusivities. With respect to triheptanoin, although some of the patents relating to triheptanoin cover aspects of composition of matter, it is possible that a competitor could develop the same or similar molecule. With respect to SA-ER, none of the patents relating to SA-ER cover composition of matter. Therefore, it is possible that a competitor could develop the same or similar molecule. If we cannot obtain and maintain effective patent rights for our product candidates, we may not be able to compete effectively and our business and results of operations would be harmed.

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

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

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

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

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

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

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

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

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

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture, or methods for treatment related to the use or manufacture of our product candidates. We have conducted freedom to operate analyses with respect to only certain of our product candidates, and therefore we do not know whether there are any third-party patents that would impair our ability to commercialize these product candidates. We also cannot guarantee that any of our analyses are complete and thorough, nor can we be sure that we have identified each and every patent and pending application in the United States and abroad that is relevant or necessary to the commercialization of our product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our product candidates may infringe.

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

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

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

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

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

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

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

Even if we are successful in achieving regulatory approval to commercialize a product candidate faster than our competitors, we may face competition from biosimilars with respect to KRN23, rhGUS, and rhPPCA. In the United States, the Biologics Price Competition and Innovation Act of 2009 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. This new pathway could allow competitors to reference data from innovative biological products 12 years after the time of approval of the innovative biological product. This data exclusivity does not prevent another company from developing a product that is highly similar to the innovative product, generating its own data, and seeking approval. Data exclusivity only assures that another company cannot rely upon the data within the innovator's application to support the biosimilar product's approval. In his proposed budget for fiscal year 2014, President Obama proposed to cut this 12-year period of exclusivity down to seven years. He also proposed to prohibit additional periods of exclusivity due to minor changes in product formulations, a practice often referred to as "evergreening." It is possible that Congress may take these or other measures to reduce or eliminate periods of exclusivity. The Biologics Price Competition and Innovation Act of 2009 is complex and only beginning to be interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning is subject to uncertainty. While it is uncertain when any such processes may be fully adopted by the FDA, any such processes could have a material adverse effect on the future commercial prospects for KRN23, rhGUS, and rhPPCA.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Interference proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could

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

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

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

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

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

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

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

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

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

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

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

Risks Related to Our Business Operations

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

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

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

Our business strategy focuses on the development of drugs that are eligible for FDA and EU orphan drug designation. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is intended to treat a rare disease or condition, defined as a patient population of fewer than 200,000 in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the EU, the EMA’s Committee for Orphan Medicinal Products, or COMP, grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention, or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the EU. Additionally, designation is granted for products intended for the diagnosis, prevention, or treatment of a life-threatening, seriously debilitating or serious and chronic condition when, without incentives, it is unlikely that sales of the drug in the EU would be sufficient to justify the necessary investment in developing the drug or biological product or where there is no satisfactory method of diagnosis, prevention, or treatment, or, if such a method exists, the medicine must be of significant benefit to those affected by the condition.

In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial 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 KRN23 in the United States, and rhGUS and SA-ER in the United States and Europe, we may not be the first to obtain marketing approval for any particular orphan indication due to the uncertainties associated with developing pharmaceutical products. Further, even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties can be approved for the same condition. Even after an orphan drug is approved, the FDA or EMA can subsequently approve the same drug with the same active moiety for the same condition if the FDA or EMA concludes that the later drug is safer, more effective, or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

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

As of March 31, 2014, we had 69 full-time employees. As our development and commercialization plans and strategies develop, we expect to need additional managerial, operational, sales, marketing, financial, legal, and other resources. Our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, operational mistakes, loss of business opportunities, loss of employees, and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and/or grow revenue could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize product candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth.

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

Although a substantial amount of our effort will focus on the continued clinical testing, potential approval, and commercialization of our existing product candidates, the success of our business also depends upon our ability to identify, license, discover, develop, or commercialize additional product candidates. Research programs to identify new product candidates 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 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 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 patients, the medical community, or third-party payors.

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

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

As a public company, we incur significant legal, accounting, and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, as well as rules subsequently implemented by the SEC, and The NASDAQ Global Select Market impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. In July 2010, the Dodd-Frank Wall Street Reform and Consumer Protection Act, or the Dodd-Frank Act, was enacted. There are significant corporate governance and executive compensation related

provisions in the Dodd-Frank Act that require the SEC to adopt additional rules and regulations in these areas such as "say on pay" and pay parity. Stockholder activism, the current political environment, and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate. Our management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased our legal and financial compliance costs and will make some activities more time consuming and costly. For example, being a public company could make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain our current levels of such coverage.

Additionally, the Sarbanes-Oxley Act requires, among other things, that we maintain effective internal controls for financial reporting and disclosure controls and procedures. In particular, we will be required to perform system and process evaluation and testing of our internal controls over financial reporting to allow management to report, commencing in our annual report on Form 10-K for the year ending December 31, 2014, on the effectiveness of our internal controls over financial reporting, if then required by Section 404(a) of the Sarbanes-Oxley Act. In the event we lose our eligibility as an emerging growth company, or EGC, as a result of meeting the large accelerated filing requirement as defined by the SEC, we would then be subject to the compliance requirements of Section 404(b) of the Sarbanes-Oxley Act. We could lose our EGC eligibility as early as December 31, 2015, thereby requiring compliance with Section 404(b), which would cause us to incur substantial accounting expense and expend significant management efforts. We currently do not have an internal audit group, and we will need to hire additional accounting and financial staff with appropriate public company experience and technical accounting knowledge. Moreover, if we are not able to comply with the requirements of Section 404(b) in a timely manner or if we identify or our independent registered public accounting firm identifies deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses, the market price of our stock could decline and we could be subject to sanctions or investigations by NASDAQ, the SEC, or other regulatory authorities, which would require additional financial and management resources.

For as long as we remain an EGC, we may take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies as described in the risk factor entitled "We are an 'emerging growth company,' and, due to the reduced reporting requirements applicable to emerging growth companies, certain investors may find investing in our common stock less attractive." We intend to take advantage of these exemptions from various reporting requirements but cannot guarantee that we will not be required to implement these requirements sooner than budgeted or planned and thereby incur unexpected expenses and also be subject to shorter timelines within which we must file our periodic reports; having to file our periodic reports on shorter timelines may also result in increased expense to us. Additionally, new laws and regulations, as well as changes to existing laws and regulations affecting public companies, including the provisions of the Sarbanes-Oxley Act and rules adopted by the SEC and by NASDAQ, would likely result in increased costs to us as we respond to their requirements.

Healthcare legislative reform measures may have a material adverse effect on our business and results of operations.

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

In addition, other legislative changes have been proposed and adopted in the United States since the Health Care Reform Law was enacted. On August 2, 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers up to 2% per fiscal year. On January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, or the ATRA, which, among other things, delayed for another two months the budget cuts mandated by these sequestration provisions of the Budget Control Act of 2011. On March 1, 2013, the President signed an executive order implementing sequestration, and on April 1, 2013, the 2% Medicare payment reductions went into effect. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

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

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

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, the purchase or recommendation of an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;
- federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology and Clinical Health Act, or HITECH, and its implementing regulations, which imposes certain requirements relating to the privacy, security, and transmission of individually identifiable health information;
- the federal physician sunshine requirements under the Health Care Reform Laws requires manufacturers of drugs, devices, biologics, and medical supplies to report annually to the U.S. Department of Health and Human Services information related to payments and other transfers of value to physicians, other healthcare providers, and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members and applicable group purchasing organizations; and
- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws that may apply to items or services reimbursed by any third-party payor, including commercial insurers, state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

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

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

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

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

- multiple, conflicting, and changing laws and regulations such as privacy regulations, tax laws, export and import restrictions, employment laws, regulatory requirements, and other governmental approvals, permits, and licenses;

- failure by us to obtain and maintain regulatory approvals for the use of our products in various countries;
- additional potentially relevant third-party patent rights;
- complexities and difficulties in obtaining protection and enforcing our intellectual property;
- difficulties in staffing and managing foreign operations;
- complexities associated with managing multiple payor reimbursement regimes, government payors, or patient self-pay systems;
- limits in our ability to penetrate international markets;
- financial risks, such as longer payment cycles, difficulty collecting accounts receivable, the impact of local and regional financial crises on demand and payment for our products, and exposure to foreign currency exchange rate fluctuations;
- natural disasters, political and economic instability, including wars, terrorism, and political unrest, outbreak of disease, boycotts, curtailment of trade, and other business restrictions;
- certain expenses including, among others, expenses for travel, translation, and insurance; and
- regulatory and compliance risks that relate to maintaining accurate information and control over sales 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.

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

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

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

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

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

Risks Related to Ownership of Our Common Stock

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

The market price of our common stock has been, and is likely to continue to be, volatile. We priced our initial public offering at $21 per share on January 30, 2014 and, since then, our common stock has reached a high of $69.77 per share. 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, 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, or other regulatory submission;
- the perception of limited market sizes or pricing for our product candidates;
- failure to successfully develop and commercialize our product candidates;
- post-marketing safety issues;
- failure to maintain our existing strategic collaborations or enter into new collaborations;
- failure by us or our licensors and strategic collaboration partners to prosecute, maintain, or enforce our intellectual property rights;
- changes in laws or regulations applicable to our products;
- any inability to obtain adequate product supply for our product candidates or the inability to do so at acceptable prices;
- adverse regulatory decisions;
- introduction of new products, services, or technologies by our competitors;
- failure to meet or exceed financial projections we may provide to the public;
- failure to meet or exceed the financial projections of the investment community;
- the perception of the pharmaceutical industry by the public, legislatures, regulators, and the investment community;
- announcements of significant acquisitions, strategic partnerships, joint ventures, or capital commitments by us, our strategic collaboration partner, or our competitors;
- disputes or other developments relating to proprietary rights, including patents, litigation matters, and our ability to obtain patent protection for our technologies;
- additions or departures of key scientific or management personnel;
- significant lawsuits, including patent or stockholder litigation;
- if securities or industry analysts do not publish research or reports about our business, or if they issue an adverse or misleading opinion regarding our stock;
- 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.

Our principal stockholders and management own a significant percentage of our stock and may be able to exert significant control over matters subject to stockholder approval.

As of May 7, 2014, our executive officers, directors, five percent stockholders, and their affiliates beneficially owned approximately 48% of our voting stock. Therefore, these stockholders may have the ability to influence us through their ownership positions, which may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may believe are in your best interest as one of our stockholders.

We are an "emerging growth company" and, due to the reduced reporting requirements applicable to emerging growth companies, certain investors may find investing in our common stock less attractive.

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. For as long as we continue to be an EGC, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not EGCs, including not being required to comply with the auditor attestation requirements of Section 404(b) of the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. We could be an EGC for up to five years from the pricing of our initial public offering, although circumstances could cause us to lose that status earlier, including if we have total annual gross revenue of $1.0 billion or more during any fiscal year before that time or if we issue more than $1.0 billion in non-convertible debt during any three-year period before that time, in which we would cease to be an EGC immediately, or on the date which we become a large accelerated filer, as defined by the SEC, in which case we would no longer be an EGC. We would become a large accelerated filer, as currently defined, if the market value of our common stock held by non-affiliates exceeds $700.0 million as of any June 30 of any year in which we have been a public company for at least 12 calendar months. We cannot predict if investors will find our common stock less attractive because we may rely on this exemption. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall.

If our existing stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market after the lock-up and other legal restrictions on resale discussed in this report lapse, the market price of our common stock could decline. As of May 7, 2014, we had a total of 30,035,894 shares of common stock outstanding. After the lock-up agreements pertaining to our initial public offering expire on July 29, 2014, up to an additional 23.3 million shares of common stock will be eligible for sale in the public market, of which approximately 17.0 million shares are held by directors, executive officers and other affiliates and will be subject to the manner of sale, volume limitations, and public reporting requirements of Rule 144 under the Securities Act of 1933, as amended, or the Securities Act. The lead underwriters may, however, in their sole discretion, permit our officers, directors, and other stockholders who are subject to these lock-up agreements to sell shares prior to the expiration of the lock-up agreements.

In addition, as of May 7, 2014, approximately 5.5 million shares of common stock that are either subject to outstanding options, reserved for future issuance under our equity incentive plans, employee stock purchase plan, or subject to outstanding warrants will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules, the lock-up agreements, and Rule 144 and Rule 701 under the Securities Act. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the market price of our common stock could decline.

The holders of approximately 19.6 million shares of our common stock, or 20.0 million including the shares underlying outstanding warrants, will be entitled to rights with respect to the registration of their shares under the Securities Act, subject to the lock-up agreements described above. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares purchased by affiliates. Any sales of securities by these stockholders could have a material adverse effect on the market price of our common stock.

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

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

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

Pursuant to our 2014 Employee Stock Purchase Plan, or 2014 ESPP, eligible employees can acquire shares of our common stock at a discount to the prevailing market price, and an aggregate of 600,000 shares are 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 (beginning January 1, 2015) by the lesser of 1,200,000 shares or 1% of all shares of our capital stock outstanding as of December 31 of the prior

calendar year, subject to the ability of our compensation committee to take action to reduce the size of the increase in any given year. If our board of directors elects to increase the number of shares available for future grant under the 2014 Plan or the 2014 ESPP, our stockholders may experience additional dilution, which could cause our stock price to fall.

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

We have incurred substantial losses during our history and do not expect to become profitable in the near future and we may never achieve profitability. To the extent that we continue to generate taxable losses, unused losses will carry forward to offset future taxable income, if any, until such unused losses expire. Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an "ownership change," generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards, or NOLs, and other pre-change tax attributes (such as research tax credits) to offset its post-change income may be limited. We may experience ownership changes in the future as a result of subsequent shifts in our stock ownership. As a result, if we earn net taxable income, our ability to use our pre-change net operating loss carryforwards to offset U.S. federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

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. Although we have paid dividends to our holders of preferred stock in the past, including a $4.3 million cash dividend paid in connection with our IPO in February 2014, all dividends paid were agreed to at the time of the private placement financings. We currently intend to retain all available funds and any future earnings, if any, for the development, operation, and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to stockholders will therefore be limited to the appreciation of their stock.

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

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

- authorize "blank check" preferred stock, which could be issued by our board of directors without stockholder approval and may contain voting, liquidation, dividend, and other rights superior to our common stock;
- create a classified board of directors whose members serve staggered three-year terms;
- specify that special meetings of our stockholders can be called only by our board of directors or the chairperson of our board of directors;
- prohibit stockholder action by written consent;
- establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors;
- provide that our directors may be removed only for cause;
- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum;
- specify that no stockholder is permitted to cumulate votes at any election of directors;
- expressly authorize our board of directors to modify, alter or repeal our amended and restated by-laws; and
- require holders of 75% of our outstanding common stock to amend specified provisions of our amended and restated certificate of incorporation and amended and restated by-laws.

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

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

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

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

Unregistered Sales of Equity Securities

During the three months ended March 31, 2014, we granted options in unregistered transactions to purchase an aggregate of 144,925 shares of common stock at a weighted-average exercise price of $21.00 per share to our employees and non-employee directors. During such period, options were exercised in unregistered transactions to purchase 46,700 shares of common stock for cash consideration in the aggregate amount of $27,000. The sales of the above securities were exempt from registration under Rule 701 promulgated under the Securities Act, as transactions pursuant to a compensatory benefit plan or a written contract relating to compensation.

Use of Proceeds

On January 30, 2014, our registration statements on Form S-1 (File Nos. 333-192244 and 333-193675) relating to the IPO of our common stock was declared effective by the SEC. The shares began trading on The NASDAQ Global Select Market on January 31, 2014. The public offering price of the shares sold in the offering was $21.00 per share. The IPO closed on February 5, 2014 and included 6,624,423 shares of common stock, which included 864,054 shares of common stock issued pursuant to the over-allotment option granted to the underwriters. We received total proceeds from the offering of $129.4 million, net of underwriting discounts and commissions of $9.7 million. After deducting offering expenses of approximately $3.3 million, a dividend of $4.3 million payable to the preferred stock holders, net proceeds were $121.7 million. Upon the closing of the IPO, all shares of convertible preferred stock then outstanding converted into 19,598,486 shares of common stock.

The net proceeds from the offerings described above have been used and will be used, together with our cash, cash equivalents and short-term investments, to fund continued advancement of our KRN23, rhGUS, LC-FAOD, Glut 1 DS, SA-ER, and pre-clinical programs, with the balance to be used to fund working capital, capital expenditures and other general corporate purposes, which may include in-licenses, acquiring, or investing in additional businesses, technologies, products, or assets the acquisition or licensing of other products, businesses or technologies.

There has been no material change in the planned use of proceeds from our initial public offering as described in our prospectus dated January 31, 2014, filed with the SEC pursuant to Rule 424(b)(4) of the Securities Act.

ITEM 3. DEFAULTS UPON SENIOR SECURITIES

None.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

ITEM 5. OTHER INFORMATION

None.

Item 6. EXHIBITS

Exhibits

3.1	Amended and Restated Certificate of Incorporation of Ultragenyx Pharmaceutical Inc.[1]
3.2	Ultragenyx Pharmaceutical Inc. Amended and Restated Bylaws.[2]
10.28	Addendum #3 to the Lease by and between Condiotti Enterprises, Inc. and Ultragenyx Pharmaceutical Inc.[3]
31.1	Certification of Principal Executive Officer Required Under Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as amended.
31.2	Certification of Principal Financial Officer Required Under Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as amended.
32.1	Certification of Principal Executive Officer and Principal Financial Officer Required Under Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, and 18 U.S.C. 1350.
101.INS	XBRL Instance Document (1)
101.SCH	XBRL Taxonomy Extension Schema Document (1)
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document (1)
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document (1)
101.LAB	XBRL Taxonomy Extension Labels Linkbase Document (1)
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document (1)

1 Incorporated by reference to Exhibit 3.1 to the Form 8-K filed on February 5, 2014.
2 Incorporated by reference to Exhibit 3.2 to the Form 8-K filed on February 5, 2014.
3 Incorporated by reference to Exhibit 10.1 to the Form 8-K filed on February 25, 2014.

(1) Pursuant to applicable securities laws and regulations, we are deemed to have complied with the reporting obligation relating to the submission of interactive data files in such exhibits and are not subject to liability under any anti-fraud provisions of the federal securities laws as long as we have made a good faith attempt to comply with the submission requirements and promptly amend the interactive data files after becoming aware that the interactive data files fail to comply with the submission requirements. In accordance with Rule 406T of Regulation S-T, the information in these exhibits is furnished and deemed not filed or a part of a registration statement or prospectus for purposes of Sections 11 or 12 of the Securities Act, is deemed not filed for purposes of Section 18 of the Exchange Act of 1934, and otherwise is not subject to liability under these sections and shall not be incorporated by reference into any registration statement or other document filed under the Securities Act, except as expressly set forth by specific reference 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: May 12, 2014

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

Date: May 12, 2014

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

Date: May 12, 2014

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

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)) 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) (Paragraph omitted pursuant to SEC Release Nos. 33-8238/34-47986 and 33-8392/34-49313);

   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: May 12, 2014

/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)) 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) (Paragraph omitted pursuant to SEC Release Nos. 33-8238/34-47986 and 33-8392/34-49313);

   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: May 12, 2014

/s/ Shalini Sharp
Shalini Sharp
Chief Financial Officer and Senior 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 March 31, 2014 (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 Senior 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: May 12, 2014

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

Dated: May 12, 2014

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