Ultragenyx Pharmaceutical Inc.
Form 10-Q
November 10, 2015

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, DC 20549

FORM 10-Q

(Mark One)

x QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934.
For the quarterly period ended September 30, 2015

OR

¨ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934.
For the transition period from to .

Commission File No. 001-36276

ULTRAGENYX PHARMACEUTICAL INC.

(Exact name of registrant as specified in its charter)

Delaware	27-2546083
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

60 Leveroni Court, Novato, California	94949
(Address of principal executive offices)	(Zip Code)

(415) 483-8800

(Registrant's telephone number, including area code)

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

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

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

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

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

As of November 4, 2015, the registrant had 38,834,703 shares of common stock issued and outstanding.

ULTRAGENYX PHARMACEUTICAL INC.

FORM 10-Q FOR THE QUARTER ENDED SEPTEMBER 30, 2015

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q contains forward-looking statements that involve risks and uncertainties. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. All statements other than statements of historical facts contained in this Quarterly Report on Form 10-Q are forward-looking statements. In some cases, you can identify forward-looking statements by words such as “anticipate,” “believe,” “contemplate,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “seek,” “should,” “target,” “will,” “would,” or the negative of these w 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.

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PART I. FINANCIAL INFORMATION

Item 1. Financial Statements

ULTRAGENYX PHARMACEUTICAL INC.

CONDENSED CONSOLIDATED BALANCE SHEETS

(Unaudited)

(In thousands, except share and per share amounts)

	September 30, 2015	December 31, 2014
Assets		
Current assets:		
Cash and cash equivalents	$166,686	$ 24,324
Short-term investments	281,697	163,163
Prepaid expenses and other current assets	12,324	5,929
Total current assets	460,707	193,416
Property and equipment, net	6,285	3,033
Restricted cash	912	744
Long-term investments	133,492	—
Other assets	734	774
Total assets	$602,130	$ 197,967
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$4,422	$ 4,857
Accrued liabilities	20,148	7,575
Deferred rent—current portion	163	85
Total current liabilities	24,733	12,517
Other liabilities	634	505
Total liabilities	25,367	13,022
Commitments and contingencies (Note 9)		
Stockholders' equity:		
Preferred stock, par value of $0.001 per share—25,000,000 shares authorized; nil outstanding as of September 30, 2015 and December 31, 2014	—	—
Common stock, par value of $0.001 per share—250,000,000 shares authorized; 38,822,177 and 31,934,682 shares issued and outstanding as of September 30, 2015 and	39	32

December 31, 2014		
Additional paid-in capital	806,202	324,128
Accumulated other comprehensive loss	(39)	(174)
Accumulated deficit	(229,439)	(139,041)
Total stockholders' equity	576,763	184,945
Total liabilities and stockholders' equity	$602,130	$ 197,967

See accompanying notes.

ULTRAGENYX PHARMACEUTICAL INC.

CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS

(Unaudited)

(In thousands, except share and per share amounts)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2015	2014	2015	2014
Operating expenses:				
Research and development	$29,704	$12,854	$70,172	$32,446
General and administrative	10,232	2,981	21,408	7,389
Total operating expenses	39,936	15,835	91,580	39,835
Loss from operations	(39,936)	(15,835)	(91,580)	(39,835)
Other income (expense), net:				
Interest income	673	171	1,402	413
Other expense, net	31	(185)	(220)	(3,642)
Total other income (expense), net	704	(14)	1,182	(3,229)
Net loss	$(39,232)	$(15,849)	$(90,398)	$(43,064)
Net loss attributable to common stockholders	$(39,232)	$(15,849)	$(90,398)	$(47,872)
Net loss per share attributable to common stockholders, basic and diluted	$(1.03)	$(0.50)	$(2.51)	$(1.73)
Shares used in computing net loss per share attributable to common stockholders, basic and diluted	38,268,632	31,631,385	36,086,598	27,697,137

See accompanying notes.

ULTRAGENYX PHARMACEUTICAL INC.

CONDENSED CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS

(Unaudited)

(In thousands)

	Three Months Ended		Nine Months Ended	
	September 30,		September 30,	
	2015	2014	2015	2014
Net loss	$(39,232)	$(15,849)	$(90,398)	$(43,064)
Other comprehensive income:				
Unrealized gain (loss) on available-for-sale securities	170	(70)	135	(129)
Total comprehensive loss	$(39,062)	$(15,919)	$(90,263)	$(43,193)

See accompanying notes.

ULTRAGENYX PHARMACEUTICAL INC.

CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS

(Unaudited)

(In thousands)

	Nine Months Ended September 30,	
	2015	2014
Operating activities:		
Net loss	$(90,398)	$(43,064)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	904	472
Amortization of premium (discount) on investment securities, net	3,700	2,444
Stock-based compensation	15,395	3,393
Revaluation of convertible preferred stock warrant liability	—	3,324
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(6,395)	(3,699)
Other assets	40	(462)
Accounts payable	(544)	2,693
Accrued liabilities and other liabilities	11,765	2,719
Net cash used in operating activities	(65,533)	(32,180)
Investing activities:		
Purchase of property and equipment	(3,032)	(1,696)
Purchase of investments	(477,321)	(160,942)
Proceeds from the sale of investments	63,310	3,003
Proceeds from maturities of investments	158,420	53,509
Increase in restricted cash	(168)	(293)
Net cash used in investing activities	(258,791)	(106,419)
Financing activities:		
Proceeds from issuance of common stock, net	466,686	188,905
Payment of preferred stock dividend	—	(4,346)
Net cash provided by financing activities	466,686	184,559
Net increase in cash and cash equivalents	142,362	45,960
Cash and cash equivalents at beginning of period	24,324	7,427
Cash and cash equivalents at end of period	$166,686	$53,387
Supplemental disclosures of non-cash investing and financing information:		
Costs of fixed assets included in accounts payable and accrued liabilities	$1,124	$72
Reclassification of warrant liability to equity upon conversion to common stock warrants	$—	$6,743
Conversion of Series A and Series B preferred stock to common stock	$—	$129,360

See accompanying notes.

ULTRAGENYX PHARMACEUTICAL INC.

Notes to Condensed Consolidated Financial Statements

1. Organization

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

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

In February 2015, the Company completed an underwritten public offering in which the Company sold 3,450,000 shares of common stock, which included 450,000 shares of common stock purchased by the underwriters pursuant to an option granted to them in connection with the offering, at a public offering price of $54.00 per share. The total proceeds that the Company received from the offering were approximately $175.1 million, net of underwriting discounts and commissions of approximately $11.2 million. After deducting offering expenses of $0.6 million, net proceeds were $174.5 million.

In July 2015, the Company completed an underwritten public offering in which the Company sold 2,530,000 shares of common stock, which included 330,000 shares of common stock purchased by the underwriters pursuant to an option granted to them in connection with the offering, at a public offering price of $120.00 per share. The total proceeds that the Company received from the offering were approximately $286.9 million, net of underwriting discounts and commissions of approximately $16.7 million. After deducting offering expenses payable of approximately $0.2 million, net proceeds were $286.7 million.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying unaudited condensed consolidated financial statements include the amounts of the Company and our wholly-owned subsidiaries and have been prepared in accordance with U.S. 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 27, 2015 with the SEC.

The results of operations for the three and nine months ended September 30, 2015 are not necessarily indicative of the results to be expected for the year ending December 31, 2015. The condensed balance sheet as of December 31, 2014 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.

Use of Estimates

The preparation of condensed consolidated 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 study and manufacturing 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 and corporate bonds.

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. As of September 30, 2015, as a result of the Company’s offering in July 2015, investments with a maturity of one year or less from the balance sheet date are reported as short-term investments and investments with a maturity of greater than one year from the balance sheet date are reported as long-term investments. 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, net, respectively. The cost of securities sold is based on the specific-identification method. Interest on investments is included in interest income.

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 investments. The Company’s cash, cash equivalents, and 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, corporate bond issuers and other financial instruments 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. In periods when we have incurred a net loss, convertible preferred stock, options and warrants to purchase common stock and convertible preferred stock warrants are considered common stock equivalents, but have been excluded from the calculation of diluted net loss per share attributable to common stockholders, as their effect is antidilutive.

Recently Issued Accounting Pronouncements

In August 2014, the FASB issued ASU No. 2014-15, Presentation of Financial Statements — Going Concern (Subtopic 205-40): Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern, which requires management to evaluate, in connection with preparing financial statements for each annual and interim reporting period, whether there are conditions or events, considered in the aggregate, that raise substantial doubt about an entity's ability to continue as a going concern within one year after the date that the financial statements are issued and provide related disclosures. This ASU will be effective for the Company in fiscal year 2016. Early adoption is permitted. We are currently assessing the future impact of this ASU in the financial statements.

3. Fair Value Measurements

Financial assets and liabilities are recorded at fair value. The carrying amount of certain financial instruments, including cash and cash equivalents, accounts payable and accrued liabilities approximate fair value due to their relatively short maturities. Assets and liabilities recorded at fair value on a recurring basis in the condensed consolidated balance sheets are categorized based upon the level of judgment associated with the inputs used to measure their fair values. Fair value is defined as the exchange price that would be received for an asset or 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):

	September 30, 2015			
	Level 1	Level 2	Level 3	Total
Financial Assets:				
Money market funds	$149,082	$—	$ —	$149,082
Corporate bonds	—	360,073	—	360,073
Asset backed securities	—	29,784	—	29,784
U.S. Government agency securities	—	23,178	—	23,178
Commercial paper	—	7,887	—	7,887
Total financial assets	$149,082	$420,922	$ —	$570,004

	December 31, 2014			
	Level 1	Level 2	Level 3	Total
Financial Assets:				
Money market funds	$8,627	$—	$ —	$8,627
Corporate bonds	—	152,942	—	152,942
Asset backed securities	—	9,542	—	9,542
U.S. Government agency securities	—	4,485	—	4,485
Other	—	209	—	209
Total financial assets	$8,627	$167,178	$ —	$175,805

In January 2014, the Company recorded a liability in connection with a convertible preferred stock warrant liability that was classified as a Level 3 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 seven years, risk-free interest rate of 2.19% and expected volatility of 70%. 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. 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):

	Nine Months Ended September 30, 2014
Fair value, beginning of period	$ 3,419
Change in fair value recorded as a loss in other expense, net	3,324
Reclassification of warrant liability to additional paid-in capital	(6,743)
Fair value, end of period	$ —

The Company recorded $3.3 million in other expense for the nine months ended September 30, 2014, representing the change in fair value of the warrants for the period. There was no corresponding expense during the nine months ended September 30, 2015 as the preferred stock warrants were converted to common stock warrants upon the completion of the IPO and are no longer subject to remeasurement.

4.Balance Sheet Components

Cash Equivalents and Investments

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

	September 30, 2015			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Money market funds classified as cash equivalents	$149,082	$—	$—	$149,082
Corporate bonds classified as cash equivalents	5,733	—	—	5,733
Commercial paper classified as short-term investments	7,887	—	—	7,887
Corporate bonds classified as short-term investments	265,914	29	(145)	265,798
Asset backed securities classified as short-term investments	8,010	2	—	8,012
Corporate bonds classified as long-term investments	88,522	71	(51)	88,542
Asset backed securities classified as long-term investments	21,741	31	—	21,772
U.S. Government agency securities classified as long-term investments	23,154	24	—	23,178
Total	$570,043	$157	$(196)	$570,004

	December 31, 2014			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Money market funds classified as cash equivalents	$8,627	$—	$—	$8,627
Corporate bonds classified as cash equivalents	3,806	1	—	3,807

Corporate bonds classified as short-term investments	149,303	4	(172)	149,135
Asset backed securities classified as short-term investments	9,546	—	(4)	9,542
U.S. Government agency securities classified as short-term investments	4,488	1	(4)	4,485
Other classified as cash equivalents	209	—	—	209
Total	$175,979	$6	$(180)	$175,805

At September 30, 2015, the remaining contractual maturities of available-for-sale securities were less than three years. There have been no significant realized gains or losses on available-for-sale securities for the periods presented.

Accrued Liabilities

Accrued liabilities consist of the following (in thousands):

	September 30, 2015	December 31, 2014
Research and clinical study expenses	$ 8,828	$ 2,703
Payroll and related expenses	7,668	4,205
Other	3,652	667
Total accrued liabilities	$ 20,148	$ 7,575

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), which was amended in August 2015. 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 $0.1 million (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. In addition, the Company is required to make certain payments to Nobelpharma based upon achievement of certain development and approval milestones. The Company has paid $0.5 million in development milestone payments since the inception of the agreement through September 30, 2015. The remaining total aggregate payments, if all milestones are achieved by Nobelpharma, would be 200 million Yen (approximately $1.7 million based on the exchange rate at September 30, 2015). The Company will pay a mid-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 a nominal up-front fee, which was recorded as research and development expense in 2010. The Company will be required to make a milestone payment of $0.1 million 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.

AAIPharma License Agreement

In March 2011, the Company entered into a license agreement with AAIPharma Services Corp. (AAIPharma). Under the terms of this license agreement, AAIPharma 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 AAIPharma'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 AAIPharma 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 a nominal up-front fee, 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 $0.3 million 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 a nominal up-front fee, 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 $0.3 million, 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 $0.8 million.

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

The Company is accounting for the agreement as a collaboration arrangement as defined in ASC 808, Collaborative Agreements; accordingly, the Company recognized $3.4 million and $1.3 million in expenses for the three months ended September 30, 2015 and 2014, and $7.0 million and $3.3 million in expenses for the nine months ended September 30, 2015 and 2014, respectively for its share of the costs as research and development. As of September 30, 2015 and December 31, 2014, the Company had receivables in the amount of $3.5 million and $1.3 million from KHK, respectively, for this collaboration arrangement.

6. Common Stock Warrants

The table sets forth the outstanding common stock warrants for the periods presented:

Outstanding at September 30, 2015	Outstanding at December 31, 2014	Date Issued	Term	Exercise Price
83,167	83,167	June 2010	10 years	$ 3.006
—	174,651	February 2011	10 years	3.006
66,533	66,533	June 2011	10 years	3.006
149,700	324,351			

7. Stock-Based Compensation
2014 Incentive Plan

In 2014, the Company adopted the 2014 Incentive Plan (the 2014 Plan), which became effective upon the closing of the Company's IPO in February 2014. The 2014 Plan provides for automatic annual increases in shares available for grant, beginning on January 1, 2015 through January 1, 2024. As of September 30, 2015, there were 1,036,380 shares reserved under the 2014 Plan for the future issuance of equity awards. The Company also had 950,295 shares reserved for the 2014 Employee Stock Purchase Plan, for which no shares had been issued.

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 September 30,		Nine Months Ended September 30,	
	2015	2014	2015	2014
Research and development	$5,555	$1,200	$10,528	$2,557
General and administrative	2,341	452	4,867	836
Total stock-based compensation	$7,896	$1,652	$15,395	$3,393

8. 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. Prior to 2015, the Company had not provided any contributions to the plan. In 2015, the Company began to make contributions to the Plan for eligible participants, and recorded $0.2 million and $0.4 million as contribution expenses for the three and nine months ended September 30, 2015, respectively.

9. 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. If a contract with a specific vendor were to be terminated, typically 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 consolidated balance sheet.

10. 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 September 30,		Nine Months Ended September 30,	
	2015	2014	2015	2014
Numerator:				
Net loss	$(39,232)	$(15,849)	$(90,398)	$(43,064)
Accretion and dividends on convertible preferred stock	—	—	—	(4,808)
Net loss attributable to common stockholders	$(39,232)	$(15,849)	$(90,398)	$(47,872)
Denominator:				
Weighted-average shares used to compute net loss per share attributable to common stockholders, basic and diluted	38,268,632	31,631,385	36,086,598	27,697,137
Net loss per share attributable to common stockholders, basic and diluted	$(1.03)	$(0.50)	$(2.51)	$(1.73)

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 September 30,		Nine Months Ended September 30,	
	2015	2014	2015	2014
Convertible preferred stock (as if converted)	—	—	—	2,153,680
Stock options to purchase common stock	3,525,167	2,749,971	3,066,088	2,542,224
Unvested restricted stock units	163,613	11,684	96,827	3,895
Convertible preferred stock warrants (as if converted)	—	—	—	38,842
Common stock warrants	149,700	353,459	211,116	314,617
	3,838,480	3,115,114	3,374,031	5,053,258

11. Subsequent Events

Arcturus Research Collaboration and License Agreement

In October 2015, the Company entered into a Research Collaboration and License Agreement with Arcturus Therapeutics, Inc. (Arcturus). The Company and Arcturus will collaborate on the research and development of therapies for select rare diseases. As consideration for entering into the arrangement, the Company will pay Arcturus an upfront fee of $10.0 million. Arcturus will have the primary responsibility for conducting certain research services, funded by the Company, and the Company will be responsible for development and commercialization costs. The Company may elect to initiate collaborative development of up to 10 targets and may be required to make additional future payments based on the achievement of development, approval and sales milestones of up to $156.0 million per target plus mid-single to low double-digit percentage royalties on net sales.

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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, 2014.

Overview

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

Our current clinical-stage pipeline consists of two product categories: biologics, including a monoclonal antibody and 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 product candidates in clinical development for the treatment of three diseases:

- KRN23, or UX023, is an antibody targeting fibroblast growth factor 23, or FGF23, in development for the treatment of XLH, a rare genetic disease that impairs bone growth. We are developing KRN23 pursuant to our collaboration with Kyowa Hakko Kirin Co., Ltd., or KHK. KHK has completed one Phase 1 study, one Phase 1/2 study, and one longer-term Phase 1/2 study of KRN23 in adults with XLH. We initiated a Phase 2 pediatric study in July 2014. We also continue the clinical development of KRN23 in adults with XLH, where a Phase 3 study is expected to be initiated by the end of 2015.
- KRN23 is also being developed for the treatment of TIO. TIO results from typically benign tumors that produce excess levels of FGF23, which can lead to severe hypophosphatemia, osteomalacia, fractures, fatigue, bone and muscle pain, and muscle weakness. We initiated a Phase 2 study of KRN23 in adult inoperable TIO patients in March 2015.
- rhGUS, or UX003, is an enzyme replacement therapy we are developing for the treatment of mucopolysaccharidosis 7, or MPS 7, a rare lysosomal storage disease that often leads to multi-organ dysfunction, pervasive skeletal disease, and death. We completed enrollment of a Phase 3 clinical study in June 2015.

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

- UX007 is a synthetic triglyceride with a specifically designed chemical composition being studied in an open-label Phase 2 study for the treatment of LC-FAOD from which interim results were recently reported. LC-FAOD is a set

of rare metabolic diseases that prevent the conversion of fat into energy and can cause low blood sugar, muscle rupture, and heart and liver disease. The company intends to begin planning for a Phase 3 study, and further details are expected to be provided after discussions with regulatory authorities in the first half of 2016.

- UX007 is also in a Phase 2 study for the treatment of Glut1 DS, a rare metabolic disease of brain energy deficiency that is characterized by seizures, developmental delay, and movement disorder. A Phase 3 study in the movement disorder phenotype of Glut1 DS is expected to begin in mid-2016.
- Ace-ER, or UX001, is an extended-release form of aceneuramic acid in a Phase 2 extension study for the treatment of GNE myopathy, a neuromuscular disorder that causes muscle weakness and wasting. We initiated a Phase 3 study in May 2015 and filed a Marketing Authorization Application, or MAA, seeking conditional approval from the European Medicines Agency, or EMA, for the use of Ace-ER in the treatment of GNE myopathy in September 2015.

Clinical Product Candidates

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

KRN23 (UX023) for the treatment of XLH

KRN23 is a fully human monoclonal antibody administered via subcutaneous injection that is designed to bind and reduce the biological activity of fibroblast growth factor 23, or FGF23, to increase abnormally low phosphate levels in patients with X-linked hypophosphatemia, or XLH. Patients with XLH have low serum phosphate levels due to excessive phosphate loss into the urine, which is directly caused by the effect on kidney function of excess FGF23 production in bone cells. Low phosphate levels lead to poor bone mineralization and a variety of clinical manifestations, including rickets leading to bowing and other skeletal deformities, short stature, bone pain and fractures, and muscle weakness. There is no approved drug therapy or treatment for the underlying cause of XLH. Most patients are managed using frequently dosed oral phosphate replacement and vitamin D therapy, which can lead to significant side effects. Oral phosphate/vitamin D replacement therapy requires extremely close monitoring due to the potential for excessive phosphate levels and secondary increases in calcium, which can result in severe damage to the kidneys from excess calcium phosphate deposits and other complications. Additionally, some patients are unable to tolerate the regimen due to the chalky stool that results from taking large amounts of oral phosphate or the high frequency of dosing required.

In August 2013, we entered into a collaboration agreement with Kyowa Hakko Kirin Co., Ltd., or KHK, which agreement was amended in August 2015, 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.

Results from the Phase 1 single-dose study in 38 adult XLH patients were presented at the American Society for Bone and Mineral Research, or ASBMR, 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. 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. Importantly, from a safety perspective, changes were not observed in serum calcium.

Results from a four-month Phase 1/2 study in 28 adult XLH patients and subsequent twelve-month Phase 1/2 study of KRN23 in 22 patients were presented at the 2014 ICE/ENDO joint meeting of The Endocrine Society and the International Congress on Endocrinology in June 2014 and ASBMR Annual Meeting in September 2014, respectively. The data demonstrated that repeat doses of KRN23 over four months led to increases in serum phosphate, renal tubular reabsorption of phosphate, and serum vitamin D levels over the 16-month period. Increases in bone remodeling markers of bone formation and bone resorption were also observed. These data support the concept that KRN23’s impact on improving phosphate metabolism will improve bone remodeling, a critical part of creating strong, and properly-formed bones. Increases in quality of life and disability measures were also observed and we intend to objectively evaluate these in a future randomized controlled study.

KRN23 was generally safe and well tolerated over the cumulative treatment period. The most common treatment-related adverse events were injection site reaction, arthralgia (joint pain), diarrhea, restless legs syndrome, injection site erythema, injection site pain, upper abdominal pain, headache, and decreased neutrophil count (both cases of low neutrophil counts were also observed at baseline and were not associated with any significant infections). Serious adverse events were reported in three subjects but were all considered unrelated to KRN23. One patient discontinued treatment due to nephrolithiasis (kidney stones) and one patient discontinued due to restless legs syndrome. There were no clinically significant changes in parathyroid hormone, renal ultrasound or cardiac CT. Serum calcium levels did not change significantly, and mild hypercalcemia was observed intermittently in two subjects. Urinary calcium was not increased, and three subjects had only transient hypercalciuria. No anti-KRN23 antibodies were observed.

In July 2014, we announced the first patient screened and enrolled in the Phase 2 pediatric study of KRN23 in patients with XLH. In late 2014, we completed enrollment of 36 prepubertal patients. The primary objectives of the study are to identify a dose and dosing regimen and to establish the safety profile of treatment with KRN23 in pediatric XLH patients. We are also assessing preliminary clinical effects of KRN23 treatment on bone health and deformity as measured by radiographic assessments, growth, muscle strength, and motor function, as well as markers of bone health and patient-reported outcomes of pain, disability, and quality of life.

The study consists of a 16-week individual dose-titration period followed by a 48-week treatment period. The goal of the dose-titration period is to identify the individualized dose of KRN23 required to achieve stable serum phosphorus levels in the target range. Patients were divided into three cohorts of escalating starting dose levels of KRN23 with either monthly or biweekly dosing regimens. At the end of the 16-week dose-titration period, patients were allowed to continue to receive dose increases in order to reach the individually-optimized dose of KRN23 on a monthly or biweekly basis for the 48-week treatment period.

In June 2015, we released 16-week data from the Phase 2 pediatric study showing that all patients had increases in serum phosphorus levels from baseline during the 16-week period. At the end of the 16 weeks, 71% of patients receiving monthly dosing reached the normal serum phosphorus range with a mean dose of 0.84 mg/kg per treatment. At the time of the analysis, of the patients who had reached week 22, 9 out of 12 (75%) reached the normal range after further dose titration. In the biweekly dosing group, the proportion of patients reaching the normal serum phosphorus range was 50% at week 16. Of the patients who had reached week 24, 7 out of 9 (78%) reached the normal range after further dose titration. Mean increases were also observed in renal phosphate reabsorption (TmP/GFR) and in serum 1,25 dihydroxy vitamin D levels.

Per the study protocol, patients discontinued standard of care, or SOC of oral phosphate and Vitamin D therapy after the screening visit, which was 2-4 weeks prior to the baseline visit. Serum phosphorus levels were measured in 16 patients at screening and baseline. While on SOC, the mean serum phosphorus level at screening in these 16 patients was 2.40 mg/dL and after wash-out from SOC at baseline was 2.26 mg/dL, representing a mean change of 0.14 mg/dL. All 16 patients had an increase from baseline in serum phosphorus after treatment with KRN23 to a mean of 3.09 mg/dL, representing an improvement of 0.83 mg/dL compared to baseline.

No serious adverse events have been reported and there have been no discontinuations from the pediatric Phase 2 study for any reason. The most common adverse events considered to be treatment related were injection site reactions in 8 patients (22%), injection site erythema in 4 patients (11%), and injection site rash, injection site swelling, and limb pain in 3 patients (8% each). All of these treatment-related adverse events were considered mild in severity. No significant changes were observed in serum calcium, urinary calcium, or serum intact parathyroid hormone (iPTH). No patients had serum phosphorus levels above the upper limit of normal in either dosing group.

In July 2015, we released interim bone treatment data from the first 12 patients in the pediatric Phase 2 study. This interim data showed an improvement in mean rickets score after 40 weeks of treatment with KRN23. Eleven of the first 12 patients enrolled had been on SOC oral phosphate and Vitamin D therapy for an average of six years (3.3–9.4 years) prior to the baseline assessment. The mean rickets score was 1.4 at baseline using the Thacher Rickets Severity Scoring method as evaluated by a blinded expert reader and decreased to 0.6 after 40 weeks of treatment with KRN23, representing a 58% reduction in rickets score. Eight out of 11 patients with rickets at baseline demonstrated an improvement in rickets, of which three patients no longer exhibited radiographic evidence of rickets at week 40. One patient in the biweekly dosing group did not present with radiographic evidence of rickets at baseline and was excluded from the analysis.

Of the 12 patients, six received biweekly dosing and six received monthly dosing of KRN23. Of the five patients with rickets at baseline in the biweekly dosing group, 100% demonstrated improvement in rickets from a mean baseline rickets score of 1.5 to a mean score of 0.3 at week 40, representing an 80% reduction in rickets score. Of the six patients in the monthly dosing group, 50% demonstrated improvement in rickets from a mean baseline score of 1.3 to a mean score of 0.8 at week 40, representing a 38% reduction in rickets score. Two patients in the monthly dosing group did not show a change and one patient in the monthly dosing group worsened by 0.5 points.

All 12 patients had increases in serum phosphorus levels from baseline at points during the 40-week treatment period. In the biweekly dosing group (n=6), mean serum phosphorus increased by 0.70 mg/dL, from 2.78 mg/dL at baseline to 3.48 mg/dL, which is in the normal range (3.2–6.1 mg/dL). In the monthly dosing group (n=6), mean serum phosphorus at peak increased by 1.06 mg/dL, from 2.42 mg/dL at baseline to 3.48 mg/dL. The monthly dosing patients showed a decrease to the trough level before the next dose, unlike the biweekly regimen which showed stable phosphate levels. Increases in renal phosphate reabsorption (TmP/GFR) and in serum 1,25 dihydroxy vitamin D levels were observed in all 12 patients.

No serious adverse events have been reported in the study to date and there have been no discontinuations from the study for any reason. For the 12 patients who had reached 40 weeks at the time of the interim analysis, the most common adverse events considered to be treatment related were injection site reactions. All of the treatment-related adverse events were considered mild in severity.

No significant changes were observed in serum calcium, urinary calcium, or serum intact parathyroid hormone (iPTH) in the 12 patients. None of the patients had serum phosphorus levels above the upper limit of normal in either dosing group. Safety data on renal ultrasounds, echocardiograms, or immune response to KRN23 are not yet available.

Additional data from the pediatric Phase 2 study, including radiographic assessments, through 40 weeks of treatment for 36 patients are expected to be available in the fourth quarter of 2015. We are expanding the pediatric Phase 2 study to enroll approximately 50 patients. The radiographic assessments through 40 weeks for the fully expanded patient group are expected to be available in mid-2016.

Depending on the final results of our Phase 2 pediatric study, we intend to conduct a Phase 3 pediatric study. In our meetings with the United States Food and Drug Administration, or FDA, and EMA, the regulatory agencies agreed that blinded radiographic assessments of changes in bone abnormalities, i.e. rickets and bowing, and changes in growth may be used as primary endpoint measures in pediatric patients. The FDA also indicated that a Phase 3 study in pediatric patients could be open-label, but recommended inclusion of a standard of care control arm for comparison on a non-inferiority basis. We expect that the final design of a pediatric Phase 3 study would be determined once sufficient safety and efficacy data are available and after further consultation with the FDA. In discussions with the EMA, the agency indicated that a filing for conditional approval may be possible based on data from the 40-week interim analysis from the pediatric Phase 2 study and from the completed Phase 1/2 and ongoing Phase 2b studies in adults, provided that there is a positive benefit-risk profile and with the obligation to conduct confirmatory studies. We will determine whether to file for conditional approval after we evaluate the pediatric Phase 2 40-week data.

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. This is consistent with 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 are also continuing to develop KRN23 in adults with XLH. We initiated a long-term, open-label Phase 2b extension study of KRN23 in adult XLH patients who had previously participated in the studies conducted by KHK. Based on discussions with the FDA and EMA, we plan to initiate a Phase 3 randomized, double-blind, placebo-controlled study in approximately 120 adult XLH patients and a Phase 3 open-label bone biopsy study in evaluating osteomalacia in approximately ten adult XLH patients by the end of 2015. The planned primary endpoint for the larger study will be serum phosphorus levels at 24 weeks. We expect that the Brief Pain Inventory patient-reported outcome will be a key secondary endpoint.

KRN23 (UX023) for the treatment of TIO

We are also developing KRN23 for the treatment of tumor-induced osteomalacia, or TIO. TIO results from typically benign tumors that produce excess levels of FGF23, which can lead to severe hypophosphatemia, osteomalacia, bone fractures, fatigue, bone and muscle pain, and muscle weakness. There are cases in which resection of the tumor is not feasible or recurrence of the tumor occurs after resection. In patients for whom the tumor is inoperable, the current standard of care consists of oral phosphate and/or vitamin D replacement. The efficacy of this treatment is often limited, as it does not treat the underlying disease and its benefits must be balanced with monitoring for potential risks such as nephrocalcinosis, hypercalciuria, and hyperparathyroidism. We are enrolling patients in an open-label, dose-finding Phase 2 clinical study. Interim data from the Phase 2 study are expected in early 2016.

This Phase 2 study will evaluate safety and efficacy in approximately six adult inoperable patients. The primary objectives of the study are to establish the dose and safety profile of treatment with KRN23 in TIO patients. Preliminary clinical effects of KRN23 treatment will be evaluated by radiographic assessments, muscle strength, walking ability, and patient-reported measures of pain, disability, and quality of life. Markers of bone health and changes in serum phosphorus and other biochemical measures will also be followed.

The study will consist of a 16-week individual dose-titration period followed by a 32-week treatment period. The goal of the dose-titration period is to identify the individualized dose of KRN23 required to achieve stable serum phosphorus levels in the target range. Patients will receive subcutaneous injections of KRN23 once every four weeks.

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

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

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

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

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

We initiated a Phase 3 global, randomized, placebo-controlled, blind-start clinical study in December 2014. The Phase 3 study is assessing the efficacy and safety of rhGUS in 12 patients between five and 35 years of age. Patients are randomized to one of four groups. One cohort begins rhGUS therapy immediately, while the other three start on placebo and cross over to rhGUS at different predefined time points in a blinded manner. This study design generates treatment data from all 12 patients. Based on data from the Phase 1/2 study, patients will be dosed with 4 mg/kg of rhGUS every other week for up to a total of 48 weeks, and all groups will receive a minimum of 24 weeks of treatment with rhGUS. The Phase 3 study fully enrolled in June 2015, and data are expected in mid-2016.

The primary objective of the study is to determine the efficacy of rhGUS as determined by the reduction in urinary GAG excretion after 24 weeks of treatment. The Phase 3 study is also evaluating as secondary endpoints the safety

and tolerability of rhGUS, pulmonary function, walking, stair climb, shoulder flexion, fine and gross motor function, hepatosplenomegaly, cardiac size and function, visual acuity, patient and caregiver assessment of most significant clinical problems, global impressions of change, a multi-domain responder index, and other endpoints.

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

In August 2015 we initiated a study of rhGUS in MPS 7 patients under the age of five years, including potentially younger infants born with hydrops fetalis. These hydropic infants can die within a few months to one year of birth, but enzyme replacement therapy might be able to reduce GAG storage and improve health in these patients. The Phase 2 open-label study will assess the safety, tolerability, and efficacy of rhGUS in up to seven pediatric patients under five years old. Interim data from the study are expected by the end of 2016.

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

UX007 for the treatment of LC-FAOD

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

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

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

In October 2015, we reported interim data on the acute effects of UX007 that was being evaluated in a Phase 2 study in LC-FAOD patients. The study was single-arm open-label and evaluated 29 pediatric and adult patients across three main symptom groups (musculoskeletal, liver/hypoglycemia, and cardiac). Patients needed to have moderate to severe FAOD with significant disease in at least one of these domains or a frequent medical events history in order to enroll. The study began with a four-week run-in period to assess baseline data while on the standard of care therapy including MCT oil, if applicable. Patients on MCT oil then discontinued it and were followed to evaluate the effects of UX007 treatment over 24 weeks on several endpoints, including cycle ergometry performance, 12-minute walk test, liver disease/hypoglycemia, cardiac disease, and quality of life. The 24-week analysis mainly evaluated the acute effects of UX007 on the musculoskeletal aspects of the disease. Patients who opted to continue will be treated for a total of 78 weeks, and rates of major medical events, such as rhabdomyolysis, hypoglycemia and cardiac events, will be

monitored and compared to rates for the two years prior to treatment with UX007. The study planned to evaluate the safety and tolerability of UX007 and to determine both the appropriate patient population as well as endpoints for evaluation in a Phase 3 study. The majority of patients enrolled presented with musculoskeletal disease compared to a limited number who presented with liver and cardiac symptoms. Patients spanned a wide age range from ten months to 58 years old. Prior to initiating treatment with UX007, 27 of the 29 patients were on the standard of care MCT oil therapy. UX007 was then titrated to a target dose of 25-35% of total daily caloric intake. The average dose of UX007 through 24 weeks was 30% of total daily caloric intake.

Improvements were observed in both measures of exercise tolerance (cycle ergometry and 12 minute walk test) in musculoskeletal patients who performed the tests. The three areas of evaluation with cycle ergometry included workload (measured in watts produced at a fixed heart rate), respiratory exchange ratio, or RER, a measure of energy supply, and duration of cycling. Patients showed improvements in both workload and duration and no change in RER. At week 24, seven patients (who qualified by age and performed the test at baseline) produced a 60% increase in watts over baseline representing a mean increase of +446.8 watts (median: +127.5) from a baseline of 744.6 watts. None of the patients who completed all 40 minutes of the cycle ergometry test at baseline and at week 24 had a reduced duration. Eight qualified patients demonstrated a mean increase of +188 meters (median: 93.5) from a baseline mean of 673.4 meters in the 12-minute walk test. These patients experienced an increase in exercise efficiency during the walk test as evidenced in an improvement in the mean energy expenditure index. The data on the 12 minute walk test and cycle ergometry together support an improvement in muscle function and exercise efficiency in a small number of patients that would need to be confirmed in larger controlled studies. Patients with liver/hypoglycemia and cardiac disease were limited, 3 and 2 respectively, but they qualified for entry due to frequent history of events and will contribute to the event rate measurement over 78 weeks.

Overall major medical events appeared to decrease in the 25 patients who completed the 24 weeks of treatment when compared to the reported event rate in these patients in the 18-24 months prior to treatment with UX007. These data are preliminary and require

significantly more time for proper evaluation at the 78 week time-point. The major medical event rate aggregates events related to hypoglycemia, rhabdomyolysis, and cardiomyopathy.

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

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

We are planning for a Phase 3 study in LC-FAOD patients based on these interim Phase 2 data. We intend to provide an update on design and timing after completing discussions with the regulatory authorities expected to occur in the first half of 2016.

UX007 for the treatment of Glut1 DS

We are also developing UX007 for patients with glucose transporter type-1 deficiency syndrome, or 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, Glut1 DS patients are considered relatively refractory to antiepileptic drugs with only approximately 8% achieving seizure control on antiepileptic drugs alone. There are currently no antiepileptic drugs approved specifically for patients with Glut1 DS.

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

In March 2014, we initiated a Phase 2 global, randomized, double-blind, placebo-controlled, parallel-group clinical study that may enroll up to 40 patients who are currently not fully compliant with ketogenic diet and continue to have seizures. The primary efficacy objective is the reduction in frequency of seizures compared to placebo following a 6-week baseline period and subsequent 8-week placebo-controlled treatment period. Other efficacy objectives include cognitive function and movement disorder. The blinded treatment period will be followed by an open-label extension

period in which patients will be treated with UX007 through week 52. Enrollment in the study has been slower than we originally anticipated due to the rare nature of the disease as well as the inclusion criteria of the study; the study is enrolling patients who are not currently on or compliant with the ketogenic diet and who have a minimum baseline seizure rate. Based on published results and in order to accelerate enrollment, we have amended the enrollment criteria to also include patients with only absence seizures.

In April 2015, positive data from an investigator-sponsored study of UX007 for the treatment of movement disorders associated with Glut1 DS were presented at the American Academy of Neurology Annual Meeting. The data showed a statistically significant 90% reduction in movement disorder events after treatment with UX007 (p=0.028) and a statistically significant increase in events after withdrawal from treatment with UX007 (p=0.043). Based on the study results, we intend to initiate a company-sponsored clinical study of UX007 in the Glut1 DS movement disorder phenotype and we expect to discuss the details of final study design with the FDA in the second half of 2015.

Following an End-of-Phase 2 meeting with the FDA, in November 2015 we announced an update to our development plan for UX007 in Glut1 DS patients. We now plan to initiate a Phase 3 study in Glut1 DS patients with the movement disorder phenotype in mid-2016. The ongoing Phase 2 study in patients with the seizure phenotype will continue to enroll up to 40 patients as the movement disorder study progresses. If the data are positive, the two studies are intended to support an NDA filing for the treatment of Glut1 DS. The Phase 3 movement disorder study is intended to be a randomized, double-blind, placebo-controlled, double cross-over study. The primary endpoint will be an assessment of the impact of UX007 on movement disorder events as recorded by a patient diary that will be further refined in discussions with the FDA. The company will continue enrollment of up to 40 patients in the randomized placebo-controlled Phase 2 seizure study. We will no longer conduct an interim analysis of the current Phase 2 study in the seizure phenotype, which will allow us to preserve the integrity of the Phase 2 study and maximize its utility from a regulatory perspective.

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

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

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

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

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

We initiated a randomized, double-blind, placebo-controlled 48-week pivotal Phase 3 study of Ace-ER in approximately 80 patients with GNE myopathy in May 2015. The FDA agreed with the Phase 3 study design, including the primary endpoint of a composite of upper extremity muscle strength, with supportive secondary endpoint data from a patient-reported outcome, both of which were studied in the Phase 2 study. Data from the Phase 3 study are expected in the first half of 2017.

In October 2015 we announced the filing and acceptance of an MAA seeking conditional approval from the EMA for the use of six grams per day of Ace-ER tablets in the treatment of GNE myopathy. A decision from the European Commission is expected in the second half of 2016.

Preclinical Pipeline

rhPPCA (UX004) for the treatment of galactosialidosis

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

Collaboration with Arcturus Therapeutics, Inc. for mRNA therapeutics

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

Other preclinical programs

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

Financial Operations Overview

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

We have never been profitable and have incurred net losses in each year since inception. Our net losses were $39.2 million and $15.8 million for the three months ended September 30, 2015 and 2014, and $90.4 million and $43.1 million for the nine months ended September 30, 2015 and 2014, respectively. Substantially all of our net losses have resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations.

Revenue

To date, we have not generated any revenue. We do not expect to receive any significant revenue until we obtain regulatory approval for any product candidates that we develop and then commercialize them or 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

Other expense primarily consists of gains and losses resulting from the remeasurement of our convertible preferred stock warrant liability. We continued to record 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, and we will no longer record any related periodic 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 nine months ended September 30, 2015, 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 and nine months ended September 30, 2015 and 2014:

Research and Development Expenses (dollars in thousands)

	Three Months Ended September 30,	Dollar	%

	2015	2014	Change	Change
Development candidate:				
KRN23 (XLH)	$4,321	$1,032	$3,289	319%
KRN23 (TIO)	282	—	282	*
rhGUS	5,130	3,609	1,521	42%
UX007 (LC-FAOD)	4,198	1,946	2,252	116%
UX007 (Glut 1 DS)	2,860	837	2,023	242%
Ace-ER	7,753	3,237	4,516	140%
Other research and development costs	5,160	2,193	2,967	135%
Total research and development expenses	$29,704	$12,854	$16,850	131%

	Nine Months Ended September 30, 2015	2014	Dollar Change	% Change
Development candidate:				
KRN23 (XLH)	$8,524	$3,115	$5,409	174%
KRN23 (TIO)	643	—	643	*
rhGUS	13,709	6,669	7,040	106%
UX007 (LC-FAOD)	8,971	6,042	2,929	48%
UX007 (Glut 1 DS)	6,152	3,230	2,922	90%
Ace-ER	18,348	8,102	10,246	126%
Other research and development costs	13,825	5,288	8,537	161%
Total research and development expenses	$70,172	$32,446	$37,726	116%

Research and development expenses increased $16.9 million and $37.7 million for the three months and nine months ended September 30, 2015, compared to the same period in 2014. The increase in research and development expenses above is primarily due to:

- for KRN23 (XLH), an increase of $3.3 million and $5.4 million for the three months and nine months ended September 30, 2015, respectively, related to the continued development of our clinical program and other development planning and regulatory activities, net of KHK reimbursement;
- for KRN23 (TIO), an increase of $0.3 million and $0.6 million for the three months and nine months ended September 30, 2015, respectively, related to the continued development of our adult TIO study and other development planning and regulatory activities, net of KHK reimbursement;
- for rhGUS, an increase of $1.5 million and $7.0 million for the three months and nine months ended September 30, 2015, respectively, related to an increase in manufacturing, quality, and clinical study related activities;
- for UX007 (LC-FAOD), an increase of $2.3 million and 2.9 million for the three months and nine months ended September 30, 2015 related to clinical manufacturing and the continued development of our clinical program and support of investigator-sponsored studies across multiple diseases;
- for UX007 (Glut1 DS), an increase of $2.0 million and $2.9 million for the three months and nine months ended September 30, 2015, respectively, related to the continued development of our clinical program, including patient identification;
- for Ace-ER, an increase of $4.5 million and $10.2 million for the three months and nine months ended September 30, 2015, respectively, related to the increase in clinical, manufacturing, quality and regulatory activities for this program; and
- an increase of $3.0 million and $8.5 million for the three months and nine months ended September 30, 2015, respectively, in other research and development costs in support of our clinical product candidate pipeline and research stage programs, and certain cost allocations, including stock compensation.

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

General and Administrative Expenses (dollars in thousands)

	Three Months Ended September 30,		Dollar	%
	2015	2014	Change	Change
General and administrative	$10,232	$2,981	$7,251	243 %

	Nine Months Ended September 30,		Dollar	%
	2015	2014	Change	Change
General and administrative	$21,408	$7,389	$14,019	190 %

General and administrative expenses increased $7.3 million and $14.0 million for the three months and nine months ended September 30, 2015, respectively, compared to the same period in 2014. The increase in general and administrative expenses was primarily due to increases in commercial planning costs, professional services costs, stock-based compensation and personnel costs resulting from an increase in employees in support of our activities.

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

Interest Income (dollars in thousands)

	Three Months Ended September 30,		Dollar Change	% Change
	2015	2014		
Interest income	$673	$171	$ 502	294 %

	Nine Months Ended September 30,		Dollar Change	% Change
	2015	2014		
Interest income	$1,402	$413	$ 989	239 %

Interest income increased $0.5 million and $1.0 million for the three months and nine months ended September 30, 2015, respectively, compared to the same period in 2014, primarily due to funds invested from our underwritten public offerings in July 2015, February 2015 and July 2014.

Other Expense, net (dollars in thousands)

	Three Months Ended September 30,		Dollar Change	% Change
	2015	2014		
Other expense, net	$(31)	$185	$ (216)	-117 %

	Nine Months Ended September 30,		Dollar Change	% Change
	2015	2014		
Other expense, net	$220	$3,642	$(3,422)	-94 %

Other expense, net decreased $0.2 million and $3.4 million for the three months and nine months ended September 30, 2015, respectively, compared to the same period in 2014. The decrease during the three months ended September 30, 2015 is the result of the remeasurement of transactions denominated in foreign currencies. The decrease during the nine months ended September 30, 2015 was primarily related to the fair value remeasurement of the liability related to our convertible preferred stock warrants. There was no corresponding expense during the nine months ended September 30, 2015 as 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, $121.7 million in net proceeds from the sale of common stock in our IPO and $521.4 million in net proceeds from the sale of common stock in our underwritten public offerings. As of September 30, 2015, we had $581.9 million in available cash, cash equivalents, and investments. Our cash, cash equivalents and investments are held in a variety of interest-bearing accounts, corporate debt securities 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. In July 2015, we also completed an underwritten public offering in which we sold 2,530,000 shares of our common stock and received net proceeds of approximately $286.7 million, after deducting underwriting discounts, commissions and offering expenses.

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

	Nine Months Ended September 30,	
	2015	2014
Cash used in operating activities	$(65,533)	$(32,180)
Cash used in investing activities	(258,791)	(106,419)
Cash provided by financing activities	466,686	184,559
Net increase in cash and cash equivalents	$142,362	