Ultragenyx Pharmaceutical Inc.
Form 424B4
January 31, 2014
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Filed Pursuant to Rule 424(b)(4)

Registration Nos. 333-192244 and 333-193675

Prospectus

5,760,369 shares

Common Stock

This is an initial public offering of common stock by Ultragenyx Pharmaceutical Inc. We are selling 5,760,369 shares of common stock. The initial public offering price is $21.00 per share.

Prior to this offering, there has been no public market for our common stock. Our common stock has been approved for listing on The NASDAQ Global Select Market under the symbol RARE .

We are an emerging growth company under applicable Securities and Exchange Commission rules and will be subject to reduced public company reporting requirements.

	Per share	Total
Initial public offering price	$ 21.00	$ 120,967,749
Underwriting discounts and commissions[(1)]	$ 1.47	$ 8,467,742
Proceeds to Ultragenyx Pharmaceutical Inc., before expenses	$ 19.53	$ 112,500,007

(1) See Underwriting for additional disclosure regarding underwriting discounts, commissions and estimated offering expenses.
We have granted the underwriters an option for a period of 30 days to purchase up to 864,054 additional shares of common stock.

Investing in our common stock involves a high degree of risk. See Risk Factors beginning on page 10.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed on the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The underwriters expect to deliver the shares of common stock to investors on or about February 5, 2014.

J.P. Morgan **Morgan Stanley**

Cowen and Company

Canaccord Genuity

January 30, 2014

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We have not authorized anyone to provide you with information other than that contained in this prospectus or in any free writing prospectus prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give to you. We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or any sale of our common stock. Our business, financial condition, results of operations, and prospects may have changed since that date.

No action is being taken in any jurisdiction outside the United States to permit a public offering of our common stock or possession or distribution of this prospectus in that jurisdiction. Persons who come into possession of this prospectus in jurisdictions outside the United States are required to inform themselves about and to observe any restrictions as to this offering and the distribution of this prospectus applicable to that jurisdiction.

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PROSPECTUS SUMMARY

The items in the following summary are described in more detail later in this prospectus. This summary provides an overview of selected information and does not contain all of the information you should consider before buying our common stock. Therefore, you should read the entire prospectus carefully, especially the Risk Factors section beginning on page 10 and our financial statements and the related notes appearing at the end of this prospectus, before deciding to invest in our common stock. In this prospectus, unless the context otherwise requires, references to the Company, we, us, our, or Ultragenyx refer to Ultragenyx Pharmaceutical Inc.

Overview

We are a development-stage biopharmaceutical company focused on the identification, acquisition, development, and commercialization of novel products for the treatment of rare and ultra-rare diseases, with an initial focus on serious, debilitating metabolic genetic diseases. We focus on diseases for which the unmet medical need is high, the biology for treatment is clear, and for which there are no approved therapies. Since our inception in 2010, we have in-licensed potential treatments for five different diseases that are or we expect will be in Phase 1/2 or Phase 2 clinical studies by early 2014. Our strategy, which is predicated upon time- and cost-efficient drug development, allows us to pursue multiple programs in parallel with the goal of delivering safe and effective therapies to patients with the utmost urgency.

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

The following table summarizes our product candidate pipeline:

Our current product candidate pipeline has been either in-licensed from academic institutions or derived from partnerships with other pharmaceutical companies. Where possible, our strategy is to acquire and retain

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global commercialization rights to our products to maximize long-term value. Over time, we intend to build our own commercial organization, which we believe will be of modest size due to the relatively small number of specialists who treat patients with rare and ultra-rare diseases.

The patients we seek to treat have diseases with limited or no treatment options, and we recognize that their lives and well-being are highly dependent upon our efforts to develop new therapies. For this reason, we are passionate about developing these therapies with the utmost urgency and care. We strive to build a company that is faster, better, and smarter about advancing multiple product candidates through approval.

We were founded in April 2010 by our current President and Chief Executive Officer, Dr. Emil Kakkis, M.D., Ph.D., who is the former Chief Medical Officer of BioMarin Pharmaceutical Inc. We have assembled an experienced team with extensive drug development and commercialization capabilities, particularly in the orphan drug area. Dr. Kakkis and the team at Ultragenyx have been previously involved, at other companies, in the development and/or commercialization of many therapies approved or in development for rare metabolic genetic diseases, including Aldurazyme, Naglazyme, Kuvan, and Vimizim (BioMarin); Lumizyme/Myozyme (Sanofi-Genzyme); and asfotase alpha (Enobia; now Alexion). Our investors include, but are not limited to, the following entities, their affiliates or funds advised by them: TPG Biotech, Fidelity Biosciences (Beacon Bioventures), HealthCap, Pappas Ventures, Adage Capital Partners, L.P., Capital Research Global Investors, Columbia Wanger Asset Management, Jennison Associates LLC, BlackRock, Inc., Genzyme Corporation, Shire LLC, and Ramius LLC.

Product Candidates

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 skeletal deformity, bone pain, short stature, gross motor impairment, muscle weakness, and lower than normal bone density. There is no approved drug therapy or treatment for the underlying cause of XLH. Most patients are managed using oral phosphate replacement and vitamin D therapy, which is only partially effective at restoring bone physiology and growth and has significant side effects.

In August 2013, we formed a collaboration with Kyowa Hakko Kirin Co., Ltd., or KHK, to jointly develop and commercialize KRN23 for the treatment of XLH. KHK has conducted one Phase 1, one Phase 1/2 study and one Phase 1/2 extension study of KRN23 in adults with XLH. We expect to release data for the Phase 1/2 studies in 2014. Results from the Phase 1 single dose study demonstrated that KRN23 was well tolerated. The data suggest efficacy in increasing serum phosphate levels, while reducing urinary excretion of phosphate. We expect to continue to develop KRN23 in adults with XLH. In addition, we expect to initiate a Phase 2 pediatric study in 2014. 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.

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. There are currently no approved drug therapies for MPS 7.

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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. In December 2013 we initiated an open-label, Phase 1/2 study to evaluate the safety, tolerability, efficacy, and dose of IV administration every other week of rhGUS in four to five patients with MPS 7 who are between five and 30 years of age. The initial 12-week treatment period will be followed by a dose-titration period and a long-term extension study. We expect to receive interim data from this study in 2014. If results from the initial 12-week treatment period from this study are supportive, we plan to initiate a pivotal Phase 3 study enrolling at least 12 patients.

rhPPCA (UX004) for the treatment of galactosialidosis

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

Triheptanoin (UX007) for the treatment of LC-FAOD

We are developing triheptanoin for oral liquid administration intended as a substrate replacement therapy for patients with long-chain fatty acid oxidation disorders, or LC-FAOD. Triheptanoin is a medium-chain triglyceride of three seven-carbon fatty acids designed to provide substrate replacement for fatty acid metabolism and restore production of energy. Patients with LC-FAOD have a deficiency that impairs the ability to produce energy from fat, which can lead to depletion of all 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-chain triglyceride, or MCT, oil supplementation. Despite treatment with the current standard of care, many patients continue to suffer significant morbidity and mortality.

Triheptanoin has been studied clinically for 13 years in approximately 130 human subjects affected by a variety of diseases, including 65 patients with LC-FAOD. Multiple investigator-sponsored open-label studies suggest clinical improvements with triheptanoin treatment, even for patients who were on standard of care. We recently completed a retrospective medical record review study to assess the clinical outcome of triheptanoin treatment on LC-FAOD subjects who have been participating in a compassionate use program at the University of Pittsburgh Medical Center. The data showed that treatment with triheptanoin appeared to reduce the frequency and severity of hospitalizations previously experienced by these patients.

We licensed certain intellectual property rights relating to triheptanoin from Baylor Research Institute in September 2012. Triheptanoin is in an ongoing investigator-sponsored Phase 2 study for the treatment of LC-FAOD. We plan to initiate a prospective open-label Phase 2 study of triheptanoin treatment in approximately 30 severely affected LC-FAOD patients in early 2014. The effects of treatment on clinical and physiologic disease will be assessed in three areas: skeletal myopathy, liver disease, and cardiac disease. A principal goal of the study is to determine the appropriate clinical endpoints and patient population for testing in potential later-stage pivotal studies.

Triheptanoin (UX007) for the treatment of Glut1 DS

We are also developing triheptanoin 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

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transports glucose from blood into the brain. Because glucose is the primary source of energy for the brain, Glut1 DS results in a chronic state of energy deficiency in the brain 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. The ketogenic diet is difficult to comply with and has demonstrated limited effectiveness in the treatment of developmental delay and movement disorder.

Triheptanoin is intended as a substrate replacement therapy to provide an alternative source of energy to the brain in Glut1 DS patients. Although an open-label investigator-sponsored clinical study is ongoing and the results have not yet been reported, there are anecdotal reports of benefit in terms of reduced seizures and improved development rate in some Glut1 DS subjects taking triheptanoin. We are planning to initiate a clinical development program to study the effects of triheptanoin in Glut1 DS in the first half of 2014. We anticipate that the program will initially consist of a Phase 2 adaptive, randomized, double-blind, placebo-controlled, parallel-group study of at least 30 patients between three and 17 years of age inclusive who are currently not on, or not fully compliant with, ketogenic diet.

SA-ER (UX001) for the treatment of HIBM

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

SA-ER is intended as a substrate replacement therapy designed to address sialic acid deficiency and restore muscle function in HIBM patients. We have conducted a Phase 2 randomized, double-blind, placebo-controlled study of SA-ER in 46 HIBM patients. Top-line results after 48 weeks of treatment showed a modest increase in upper extremity muscle strength composite at the higher dose and a statistically significant difference versus the decline observed at the lower dose. A positive trend was seen in a patient-reported outcome of functional activity. The results were consistent with the 24-week analysis. SA-ER appears to be well tolerated with no serious adverse events observed to date in either dose group. We plan to continue to treat these patients in an extension study with an increased dosage of sialic acid based on the dose dependence observed at weeks 24 and 48. We anticipate that data from the extension study should be available in late 2014.

Our Strategy

Our strategy is to identify, acquire, develop, and commercialize novel products for the treatment of rare and ultra-rare diseases in the United States, the European Union, and select international markets, with the goal of becoming a leading rare disease company. The critical components of our business strategy include the following:

- Focus on rare and ultra-rare diseases with significant unmet medical need;
- Focus on diseases and therapies with clear mechanisms of action;
- Leverage our experience and relationships to in-license promising product candidates;
- Develop and commercialize multiple product candidates in parallel;
- Focus on excellent and rapid clinical and regulatory execution; and
- Seek to retain global commercialization rights to product candidates.

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Risks Associated with Our Business

Our ability to implement our business strategy is subject to numerous risks that you should be aware of before making an investment decision. These risks are described more fully in the section entitled Risk Factors immediately following this prospectus summary. These risks include, among others:

- We are a development-stage company and have a limited operating history on which to assess our business, have incurred significant losses since our inception, and anticipate that we will continue to incur significant losses for the foreseeable future;
- Even if this offering is successful, we expect that we will need to raise additional funding before we can expect to become profitable from sales of our products;
- We are heavily dependent upon the success of our product candidates, which are in the early stages of clinical development, and we cannot provide any assurance that any of our product candidates will receive regulatory approval;
- Because the target patient populations of our product candidates are small, we must be able to successfully identify patients and acquire a significant market share to achieve profitability and growth;
- The insurance coverage and reimbursement status of newly-approved orphan products is uncertain and failure to obtain or maintain adequate coverage and reimbursement for our product candidates could limit our ability to market those products and decrease our ability to generate revenue;
- If we are unable to obtain and maintain effective intellectual property rights for our technologies, product candidates, or any future product candidates, we may not be able to compete effectively in our markets; and
- Our future success depends in part upon our ability to retain our Founder, President, and Chief Executive Officer and to attract, retain, and motivate other qualified personnel.

Our Corporate Information

We were founded in April 2010 as a California corporation, and we reincorporated as a Delaware corporation in June 2011. Our principal executive offices are located at 60 Leveroni Court, Novato, CA 94949, and our telephone number is (415) 483-8800. Our web site address is www.ultragenyx.com. The information on, or that can be accessed through, our web site is not part of this prospectus. We have included our web site address as an inactive textual reference only.

We have filed trademark applications with the U.S. Patent and Trademark Office for the marks Ultragenyx and Ultragenyx Pharmaceutical, and we are developing commercial names for our product candidates. This prospectus also contains trademarks of others, including Aldurazyme®, Naglazyme®, Kuvan®, Vimizim, Lumizyme®, Myozyme® and asfotase alpha. We do not intend our use or display of other companies trade names or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

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THE OFFERING

Common stock offered by us	5,760,369 shares
Common stock to be outstanding after this offering	29,061,871 shares (or 29,925,925 shares if the underwriters exercise their option to purchase additional shares in full)
Underwriters option to purchase additional shares	864,054 shares
Use of proceeds	We estimate that the net proceeds from this offering will be approximately $109.5 million, or approximately $126.4 million if the underwriters exercise their option to purchase additional shares in full, at an initial public offering price of $21.00 per share, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. We intend to use the net proceeds from this offering, together with our existing cash, cash equivalents, and marketable securities to advance our ongoing clinical programs for KRN23, rhGUS, triheptanoin in both LC-FAOD and Glut1 DS, and SA-ER, to pay a cash dividend to holders of our preferred stock payable upon conversion of the shares to common stock, and any remaining proceeds for preclinical research, our ongoing clinical programs, working capital, and other general corporate purposes. See Use of Proceeds.
Risk factors	You should read the Risk Factors section of this prospectus for a discussion of factors to consider carefully before deciding to invest in shares of our common stock.
Directed share program	At our request, the underwriters have reserved up to 258,900 shares of our common stock offered by this prospectus for sale, at the initial public offering price, to our directors and officers and certain employees and other parties related to us. Shares purchased by our directors and officers will be subject to the 180-day lock-up restriction described in the Underwriting section of this prospectus. The number of shares of common stock available for sale to the general public will be reduced to the extent these individuals purchase such reserved shares. Any reserved shares that are not so purchased will be offered by the underwriters to the general public on the same basis as the other shares offered by this prospectus.
NASDAQ Global Select Market symbol	RARE

The number of shares of common stock to be outstanding after this offering is based on 3,703,016 shares of common stock outstanding as of September 30, 2013 and 19,598,486 additional shares of our common stock issuable upon conversion of all of our outstanding shares of preferred stock upon closing of this offering.

The number of shares of our common stock to be outstanding after this offering excludes the following:

- 1,526,772 shares of common stock issuable upon the exercise of outstanding stock options as of September 30, 2013 having a weighted-average exercise price of $0.86 per share;

353,459 shares of common stock issuable upon the exercise of outstanding warrants as of September 30, 2013 having a weighted-average exercise price of $3.006 per share;

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1,565,352 shares of common stock reserved for issuance pursuant to future equity awards under our 2011 Equity Incentive Plan, as amended, as of September 30, 2013, which will become available for issuance under our 2014 Incentive Plan after the completion of this offering;

2,250,000 shares of common stock reserved for issuance (including the above-referenced shares reserved for issuance under our 2011 Equity Incentive Plan, as amended) pursuant to future equity awards under our 2014 Incentive Plan, as well as any future increases in the number of shares of our common stock reserved for future issuance under this plan, which will become effective immediately prior to the completion of this offering; and

600,000 shares of common stock reserved for future issuance under our 2014 Employee Stock Purchase Plan, or 2014 ESPP, as well as any future increases in the number of shares of our common stock reserved for future issuance under the 2014 ESPP, which will become effective immediately prior to the completion of this offering.

Except as otherwise indicated, all information contained in this prospectus:

reflects a 1-for-3.1345 reverse stock split of our common stock that we effected on January 17, 2014;

reflects the conversion of all of our outstanding shares of preferred stock into an aggregate of 19,598,486 shares of common stock immediately prior to the completion of this offering;

assumes the effectiveness of our amended and restated certificate of incorporation and amended and restated by-laws in connection with the completion of this offering;

assumes that the underwriters do not exercise their option to purchase additional shares; and

assumes no exercise of outstanding options or warrants after September 30, 2013.

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SUMMARY FINANCIAL DATA

The following table summarizes our statements of operations and balance sheet data. We have derived the following statements of operations data for the years ended December 31, 2011 and 2012 from our audited financial statements appearing elsewhere in this prospectus. The statements of operations data for the nine months ended September 30, 2012 and 2013 and the balance sheet data as of September 30, 2013 are derived from our unaudited financial statements appearing elsewhere in this prospectus. In our opinion, these unaudited financial statements have been prepared on a basis consistent with our audited financial statements and contain all adjustments, consisting only of normal and recurring adjustments, necessary for a fair presentation of such financial data. You should read this data together with our financial statements and related notes appearing elsewhere in this prospectus and the information under the captions Selected Financial Data and Management s Discussion and Analysis of Financial Condition and Results of Operations. Our historical results are not necessarily indicative of our future results, and our operating results for the nine-month period ended September 30, 2013 are not necessarily indicative of the results that may be expected for the year ended December 31, 2013 or any other interim periods or any future year or period.

	Year Ended December 31,		Nine Months Ended September 30,	
	2011	2012	2012	2013
	(In thousands, except share and per share amounts)		(unaudited)	
Statements of Operations Data:				
Operating expenses:				
Research and development	$ 4,717	$ 12,641	$ 8,866	$ 19,625
General and administrative	1,844	3,344	2,441	3,130
Total operating expenses	6,561	15,985	11,307	22,755
Loss from operations	(6,561)	(15,985)	(11,307)	(22,755)
Interest income	4	1		157
Interest expense	(270)			
Other expense	(22)	(350)	(97)	(1,155)
Net loss	$ (6,849)	$ (16,334)	$ (11,404)	$ (23,753)
Net loss attributable to common stockholders [(1)]	$ (7,466)	$ (19,561)	$ (12,749)	$ (31,624)
Net loss per share attributable to common stockholders, basic and diluted	$ (4.62)	$ (14.20)	$ (12.35)	$ (9.70)
Shares used to compute net loss per share attributable to common stockholders, basic and diluted	1,617,384	1,377,207	1,032,159	3,260,484
Pro forma net loss per share attributable to common stockholders, basic and diluted (unaudited) [(1)]		$ (2.04)		$ (1.17)
Shares used to compute pro forma net loss per share attributable to common stockholders, basic and diluted (unaudited) [(1)]		9,935,836		23,062,827

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	As of September 30, 2013		
	Actual	Pro Forma[2] (unaudited) (in thousands)	Pro Forma as Adjusted[3]
Balance Sheet Data:			
Cash, cash equivalents and marketable securities	$ 63,657	$ 63,657	$ 168,876
Working capital	61,067	56,786	166,286
Total assets	68,592	68,592	173,811
Convertible preferred stock warrant liability	1,596		
Convertible preferred stock	118,002		
Deficit accumulated during the development stage	(56,846)	(56,846)	(56,846)
Total stockholders (deficit) equity	(56,848)	58,469	167,969

(1) See Notes 2 and 14 to our audited financial statements and Note 8 of our unaudited financial statements included elsewhere in this prospectus for an explanation of the calculations of our basic and diluted net loss per share attributable to common stockholders and pro forma net loss per share attributable to common stockholders.

(2) Pro forma to reflect (i) the conversion of all of our outstanding shares of convertible preferred stock into an aggregate of 19,598,486 shares of our common stock, (ii) the reclassification to additional paid-in capital of our preferred stock warrant liability in connection with the conversion of our outstanding preferred stock warrants into common stock warrants, and (iii) a dividend of $4.3 million payable concurrent with the conversion of our preferred stock to common stock to the holders of our preferred stock, which has been calculated as if the conversion of preferred stock into common stock occurred as of January 30, 2014, in each case, immediately prior to the completion of this offering. Since the dividend represents distributions to existing stockholders to be made from the proceeds of the offering, the pro forma balance sheet data reflects the accrual of the estimated dividend to be paid.

(3) Pro forma as adjusted to further reflect (i) the sale of 5,760,369 shares of common stock in this offering at an initial public offering price of $21.00 per share, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us and (ii) the payment of the $4.3 million dividend payable described above.

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RISK FACTORS

An investment in shares of our common stock involves a high degree of risk. You should carefully consider the following information about these risks, together with the other information appearing elsewhere in this prospectus, including our financial statements and related notes thereto, before deciding to invest in our common stock. The occurrence of any of the following risks could have a material adverse effect on our business, financial condition, results of operations and future growth prospects. In these circumstances, the market price of our common stock could decline, and you may lose all or part of your investment.

Risks Related to Our Financial Condition and Capital Requirements

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

We are a development-stage biopharmaceutical company with a limited operating history. We have incurred net losses in each year since our inception in April 2010, including net losses of $6.8 million and $16.3 million for the years ended December 31, 2011 and 2012, respectively, and $23.8 million for the nine months ended September 30, 2013. As of September 30, 2013, we had a deficit accumulated during the development stage of $56.8 million.

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

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

- continue our research and nonclinical and clinical development of our product candidates;
- expand the scope of our current clinical studies for our product candidates;
- advance our programs into more expensive clinical studies;
- initiate additional nonclinical, clinical, or other studies for our product candidates;
- change or add additional manufacturers or suppliers;
- seek regulatory and marketing approvals for our product candidates that successfully complete clinical studies;

establish a sales, marketing, and distribution infrastructure to commercialize any products for which we may obtain marketing approval;

seek to identify, assess, acquire, and/or develop other product candidates;

make milestone or other payments under any license agreements;

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- seek to maintain, protect, and expand our intellectual property portfolio;
- seek to attract and retain skilled personnel;
- create additional infrastructure to support our operations as a public company and our product development and planned future commercialization efforts; and
- experience any delays or encounter issues with any of the above, including but not limited to failed studies, complex results, safety issues, or other regulatory challenges that require longer follow-up of existing studies, additional major studies, or additional supportive studies in order to pursue marketing approval.

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

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

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

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

maintaining, protecting, and expanding our portfolio of intellectual property rights, including patents, trade secrets, and know-how; and

attracting, hiring, and retaining qualified personnel.

Even if one or more of the product candidates that we develop is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. Our expenses could increase beyond expectations if we are required by the U.S. Food and Drug Administration, or the FDA, the European Medicines Agency, or the EMA, or other regulatory agencies, domestic or foreign, to change our manufacturing processes or assays, or to perform clinical, nonclinical, or other types of studies in addition to those that we currently anticipate. In cases where we are successful in obtaining regulatory approvals to market one or more of our product candidates, our revenue will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval, the accepted price for the product, the ability to get reimbursement at any price, and whether we own the commercial rights for that territory. If the number of our

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addressable rare disease patients is not as significant as we estimate, the indication approved by regulatory authorities is narrower than we expect, or the reasonably accepted population for treatment is narrowed by competition, physician choice or treatment guidelines, we may not generate significant revenue from sales of such products, even if approved. For example, the development of KRN23, rhGUS, and triheptanoin for pediatric use is an important part of our current business strategy; if we are unable to obtain regulatory approval for the desired age ranges, our business may suffer. Additionally, if we are not able to generate revenue from the sale of any approved products, we may never become profitable.

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

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

As of September 30, 2013, our cash, cash equivalents and marketable securities were $63.7 million. We expect that our existing cash, cash equivalents and marketable securities, not including the proceeds we receive from this offering, will be sufficient to fund our current operations for at least the next 12 months; however, we expect that we will require additional capital to obtain regulatory approval for, and to commercialize, our product candidates. In addition, our operating plans may change as a result of many factors that may currently be unknown to us, and we may need to seek additional funds sooner than planned. Our future funding requirements will depend on many factors, including but not limited to:

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

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

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

Risks Related to the Discovery and Development of Our Product Candidates

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

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

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

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

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

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

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

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

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical studies;
- the population studied in the clinical program may not be sufficiently broad or representative to assure safety in the full population for which we seek approval;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from nonclinical studies or clinical studies;
- the data collected from clinical studies of our product candidates may not be sufficient to support the submission of a new drug application, or NDA, or biologics license application, or BLA, or other submission or to obtain regulatory approval in the United States or elsewhere;
- we may be unable to demonstrate to the FDA or comparable foreign regulatory authorities that a product candidate s risk-benefit ratio for its proposed indication is acceptable;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes, test procedures and specifications, or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

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

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

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical study process. The results of preclinical studies and early clinical studies of our product candidates may not be predictive of the results of later-stage clinical studies. Product candidates that have shown promising results in early-stage clinical studies may still suffer significant setbacks in subsequent registration clinical studies. For example, the safety or efficacy results generated to date in clinical studies for KRN23, triheptanoin, and SA-ER do not ensure that later clinical studies will demonstrate similar results. There is a high failure rate for drugs and biologics proceeding through clinical studies, and product candidates in later stages of clinical studies may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical studies. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical studies due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier studies. Moreover, nonclinical and clinical data are often susceptible to varying interpretations and analyses. We do not know whether any Phase 2, Phase 3, or other clinical studies we may conduct will demonstrate consistent or adequate efficacy and safety sufficient to obtain regulatory approval to market our drug candidates.

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

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

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

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

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

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

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

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical studies to demonstrate the safety and efficacy of the product candidates in humans. Clinical testing is expensive, time consuming, and uncertain as to outcome. We cannot guarantee that any clinical studies will be conducted as planned or completed on schedule, if at all. A failure of one or more clinical studies can occur at any stage of testing, and our future clinical studies may not be successful. Events that may prevent successful or timely completion of clinical development include but are not limited to:

- inability to generate sufficient preclinical, toxicology, or other *in vivo* or *in vitro* data to support the initiation of human clinical studies;
- delays in reaching a consensus with regulatory agencies on study design;
- delays in reaching agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical study sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical study sites;

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delays in obtaining required Institutional Review Board, or IRB, approval at each clinical study site;

imposition of a clinical hold by regulatory agencies, after review of an investigational new drug, or IND, application or amendment, or equivalent application or amendment, or an inspection of our clinical study operations or study sites;

delays in recruiting suitable patients to participate in our clinical studies;

difficulty collaborating with patient groups and investigators;

failure by our CROs, other third parties, or us to adhere to clinical study requirements;

failure to perform in accordance with the FDA s good clinical practices requirements, or applicable regulatory guidelines in other countries;

delays in having patients complete participation in a study or return for post-treatment follow-up;

patients dropping out of a study;

occurrence of adverse events associated with the product candidate that are viewed to outweigh its potential benefits;

changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;

the cost of clinical studies of our drug candidates being greater than we anticipate;

clinical studies of our drug candidates producing negative or inconclusive results, which may result in us deciding, or regulators requiring us, to conduct additional clinical studies or abandon drug development programs; and

delays in manufacturing, testing, releasing, validating, or importing/exporting sufficient stable quantities of our product candidates for use in clinical studies or the inability to do any of the foregoing.

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

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

Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay, or halt clinical studies and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign authorities. Patients

treated with KRN23 have experienced nausea, headache, elevated serum amylase, and back pain. Most of these adverse events were mild and no serious adverse events have been observed. Only single-dose Phase 1 data for KRN23 has been reported to date and other side effects may result from repeated dosing and/or longer-term exposure. Patients treated with triheptanoin have experienced drug-related side effects such as cramping, diarrhea, and loose stools. In addition, during a 13-year study of approximately 130 human subjects, including 65 with LC-FAOD, three serious adverse events were classified as possibly related to triheptanoin treatment (muscle cell rupture and elevated creatine kinase reported for two subjects and myoglobinuria in one subject); however, these serious adverse events can be considered typical of the underlying disease. While we have not initiated our own clinical studies for

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triheptanoin, there may be other side effects associated with its use that we discover. Additionally, patients treated with SA-ER have experienced drug-related side effects including mild gastrointestinal discomfort. Enzyme replacement therapies have been associated with infusion-associated reactions due to a developing allergy to the product, which can cause rashes, pain, significant clinical disease, or even death. Our rhGUS and rhPPCA product candidates may also cause these or similar side effects when clinical trials are initiated. Results of our studies could reveal a high and unacceptable severity and prevalence of these or other side effects. In such an event, our studies could be suspended or terminated, and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny or withdraw approval of our product candidates for any or all targeted indications.

The drug-related side effects could affect patient recruitment, the ability of enrolled patients to complete the study, or result in potential product liability claims. We currently carry product liability insurance in the amount of $5.0 million in the aggregate, and we are required to maintain product liability insurance pursuant to certain of our license agreements. We believe our product liability insurance coverage is sufficient in light of our current clinical programs; however, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business. In addition, regardless of merit or eventual outcome, product liability claims may result in impairment of our business reputation, withdrawal of clinical study participants, costs due to related litigation, distraction of management s attention from our primary business, initiation of investigations by regulators, substantial monetary awards to patients or other claimants, the inability to commercialize our product candidates, and decreased demand for our product candidates, if approved for commercial sale.

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

- regulatory authorities may withdraw approvals of such product;
- regulatory authorities may require additional warnings on the label;
- we may be required to create a Risk Evaluation and Mitigation Strategy, or REMS, plan, which could include a medication guide outlining the risks of such side effects for distribution to patients, a communication plan for healthcare providers, and/or other elements to assure safe use;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

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

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

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

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

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

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

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

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

Risks Related to our Reliance on Third Parties

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

We have relied upon and plan to continue to rely upon third-party CROs to monitor and manage data for our ongoing nonclinical and clinical programs. We rely on these parties for execution of our nonclinical and clinical studies, and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory,

and scientific standards and our reliance on the CROs does not relieve us of our regulatory responsibilities. We and our CROs and other vendors are required to comply with cGMP, current good clinical practices, or cGCP, and Good Laboratory Practices, or

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GLP, which are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area, or EEA, and comparable foreign regulatory authorities for all of our product candidates in clinical development. Regulatory authorities enforce these regulations through periodic inspections of study sponsors, principal investigators, study sites, and other contractors. If we or any of our CROs or vendors fail to comply with applicable regulations, the data generated in our nonclinical and clinical studies may be deemed unreliable and the FDA, EMA, or comparable foreign regulatory authorities may require us to perform additional nonclinical and clinical studies before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical studies comply with cGCP regulations. In addition, our clinical studies must be conducted with product produced under cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical studies, which would delay the regulatory approval process.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs or do so on commercially reasonable terms. In addition, our CROs are not our employees, and except for remedies available to us under our agreements with such CROs, we cannot control whether or not they devote sufficient time and resources to our on-going nonclinical and clinical programs. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the data they obtain is compromised due to the failure to adhere to our protocols, regulatory requirements, or for other reasons, our clinical studies may be extended, delayed, or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. CROs may also generate higher costs than anticipated. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase, and our ability to generate revenue could be delayed.

Switching or adding additional CROs involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition, and prospects.

We are dependent on KHK for the development and commercialization of KRN23 in certain major markets, and KHK s failure to commercialize KRN23 in those markets would result in a material adverse effect on our business and operating results.

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

- KHK has no obligation under our agreement to use diligent efforts to commercialize KRN23 in Europe. The timing and amount of any royalty payments we may receive under our agreement will depend on, among other things, the efforts, allocation of resources, and successful commercialization of KRN23 by KHK in Europe. Additionally, if KHK were to decide not to commercialize KRN23 in Europe, and we nevertheless wished to commercialize KRN23 in Europe, we would need to renegotiate with KHK certain terms of our agreement but may be unable to do so on reasonable terms, in a timely manner, or at all;

- the timing and amount of any royalty payments we may receive under our agreement with KHK will depend on, among other things, the efforts, allocation of resources, and successful commercialization of KRN23 by KHK in the United States and Canada under our agreement;

- KHK may change the focus of its commercialization efforts or pursue higher-priority programs;

- KHK may fail to manufacture or supply sufficient drug product of KRN23 for our development and clinical use, which could result in program delays;

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- KHK may fail to manufacture or supply sufficient drug product of KRN23 for our commercial use, if approved, which could result in lost revenue;

- KHK may elect to develop and commercialize KRN23 indications with a larger market than XLH and at a lower price, thereby reducing the profit margin on sales of KRN23 for any orphan indications, including XLH;

- if KHK were to breach or terminate the agreement with us, we would no longer have any rights to develop or commercialize KRN23 or such rights would be limited to non-terminated countries;

- KHK may terminate its agreement with us, adversely impacting our potential revenue from licensed products; and

- the timing and amounts of expense reimbursement that we may receive are uncertain, and the total expenses for which we are obligated to reimburse KHK may be greater than anticipated.

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

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

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

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

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

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

Although we have not experienced any contaminations, equipment failures, or other similar manufacturing problems, any adverse developments affecting manufacturing operations for our product candidates may result in shipment delays, inventory shortages, lot failures, withdrawals or recalls, or other interruptions in the supply of

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our product candidates. We may also have to take inventory write-offs and incur other charges and expenses for product candidates that fail to meet specifications, undertake costly remediation efforts, or seek more costly manufacturing alternatives.

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

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

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

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

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

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

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

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

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

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

Risks Related to Commercialization of Our Product Candidates

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

We focus our research and product development on treatments for rare and ultra-rare genetic diseases. Given the small number of patients who have the diseases that we are targeting, it is critical to our ability to grow and become profitable that we continue to successfully identify patients with these rare and ultra-rare genetic diseases. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on

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our beliefs and estimates. These estimates have been derived from a variety of sources, including the scientific literature, surveys of clinics, patient foundations, or market research, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these diseases. The number of patients may turn out to be lower than expected. The effort to identify patients with diseases we seek to treat is in early stages, and we cannot accurately predict the number of patients for whom treatment might be possible. Additionally, the potentially addressable patient population for each of our product candidates may be limited or may not be amenable to treatment with our product candidates, and new patients may become increasingly difficult to identify or gain access to, which would adversely affect our results of operations and our business. Further, even if we obtain significant market share for our product candidates, because the potential target populations are very small, we may never achieve profitability despite obtaining such significant market share.

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

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

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

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

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

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

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

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

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

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

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

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

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medical community. The degree of market acceptance of any of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy of the product as demonstrated in clinical studies and potential advantages over competing treatments;
- the prevalence and severity of any side effects, including any limitations or warnings contained in a product s approved labeling;
- the clinical indications for which approval is granted;
- relative convenience and ease of administration;
- the cost of treatment, particularly in relation to competing treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support and timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments; and
- sufficient third-party insurance coverage and reimbursement.

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

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

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

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

degree. It is difficult to predict what CMS will decide with respect to reimbursement for products such as ours.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in

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

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

Risks Related to Our Intellectual Property

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

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

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

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

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

Although we have a number of patents covering methods of use and certain compositions of matter, we do not have complete patent protection for our product candidates. For example, there is no patent coverage for

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KRN23 in Latin America, where we have rights to commercialize the compound. Therefore, a competitor could develop the same or similar antibody as well as other approaches that target FGF23. Additionally, none of the current intellectual property relating to rhGUS covers composition of matter, and there are currently no patents that cover rhPPCA. Therefore, it is possible that a competitor could develop the same or similar enzyme with respect to rhGUS and/or rhPPCA, subject to any regulatory exclusivities. With respect to triheptanoin, although some of the patents relating to triheptanoin cover aspects of composition of matter, it is possible that a competitor could develop the same or similar molecule. With respect to SA-ER, none of the patents relating to SA-ER cover composition of matter. Therefore, it is possible that a competitor could develop the same or similar molecule. If we cannot obtain and maintain effective patent rights for our product candidates, we may not be able to compete effectively and our business and results of operations would be harmed.

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

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

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

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

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

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

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

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

Third-party claims of intellectual property infringement may prevent or delay our development and commercialization efforts.

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

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

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

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

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

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

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

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

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

Even if we are successful in achieving regulatory approval to commercialize a product candidate faster than our competitors, we may face competition from biosimilars with respect to KRN23, rhGUS, and rhPPCA. In the United States, the Biologics Price Competition and Innovation Act of 2009 created an abbreviated approval pathway for biological products that are demonstrated to be highly similar, or biosimilar, to or interchangeable with an FDA-approved biological product. This new pathway could allow competitors to reference data from innovative biological products 12 years after the time of approval of the innovative biological product. This data exclusivity does not prevent another company from developing a product that is highly similar to the innovative product, generating its own data, and seeking approval. Data exclusivity only assures that another company cannot rely upon the data within the innovator s application to support the biosimilar product s approval. In his proposed budget for fiscal year 2014, President Obama proposed to cut this 12-year period of exclusivity down to seven years. He also proposed to prohibit additional periods of exclusivity due to minor changes in product formulations, a practice often referred to as evergreening. It is possible that Congress may take these or other measures to reduce or eliminate periods of exclusivity. The Biologics Price Competition and Innovation Act of 2009 is complex and only beginning to be interpreted and implemented by

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the FDA. As a result, its ultimate impact, implementation, and meaning is subject to uncertainty. While it is uncertain when any such processes may be fully adopted by the FDA, any such processes could have a material adverse effect on the future commercial prospects for KRN23, rhGUS, and rhPPCA.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

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

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

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

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

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

Risks Related to Our Business Operations

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

We are highly dependent on Emil D. Kakkis, M.D., Ph.D., our Founder, President, and Chief Executive Officer, the loss of whose services may adversely impact the achievement of our objectives. Dr. Kakkis could

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

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

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

In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages, and user-fee waivers. In addition, if a product receives the first FDA approval for the indication for which it has orphan designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity or where the manufacturer is unable to assure sufficient product quantity. In the European Union, orphan drug designation entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity following drug or biological product approval. This period may be reduced to six years if the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity.

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

Even though we have orphan drug designation for KRN23 in the United States, and rhGUS and SA-ER in the United States and Europe, we may not be the first to obtain marketing approval for any particular orphan indication due to the uncertainties associated with developing pharmaceutical products. Further, even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties can be approved for the same condition. Even after an orphan drug is approved, the FDA or EMA can subsequently approve the same drug with the same active moiety for the same condition if the FDA or EMA concludes that the later drug is safer, more effective, or makes

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a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

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

As of December 31, 2013, we had 59 full-time employees. As our development and commercialization plans and strategies develop, we expect to need additional managerial, operational, sales, marketing, financial, legal, and other resources. Our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, operational mistakes, loss of business opportunities, loss of employees, and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and/or grow revenue could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize product candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth.

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

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

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

a product candidate may not be accepted as safe and effective by patients, the medical community, or third-party payors.

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

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We will incur significant increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives.

As a public company, we will incur significant legal, accounting, and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act, as well as rules subsequently implemented by the Securities and Exchange Commission, or SEC, and The NASDAQ Global Select Market have imposed various requirements on public companies. In July 2010, the Dodd-Frank Wall Street Reform and Consumer Protection Act, or the Dodd-Frank Act, was enacted. There are significant corporate governance and executive compensation related provisions in the Dodd-Frank Act that require the SEC to adopt additional rules and regulations in these areas such as say on pay and pay parity. Recent legislation permits smaller emerging growth companies to implement many of these requirements over a longer period and up to five years from the pricing of this offering. We intend to take advantage of this new legislation but cannot guarantee that we will not be required to implement these requirements sooner than budgeted or planned and thereby incur unexpected expenses. Stockholder activism, the current political environment, and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time consuming and costly. For example, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain our current levels of such coverage.

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

New laws and regulations as well as changes to existing laws and regulations affecting public companies, including the provisions of the Sarbanes-Oxley Act and rules adopted by the SEC and by NASDAQ, would likely result in increased costs to us as we respond to their requirements.

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

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

care organizations, establishes annual fees and taxes on manufacturers of certain branded prescription drugs, and promotes a new Medicare Part D coverage gap discount program.

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

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

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

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, the purchase or recommendation of an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;

- federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;

- HIPAA, as amended by the Health Information Technology and Clinical Health Act, or HITECH, and its implementing regulations, which imposes certain requirements relating to the privacy, security, and transmission of individually identifiable health information;

- the federal physician sunshine requirements under the Health Care Reform Laws requires manufacturers of drugs, devices, biologics, and medical supplies to report annually to the U.S. Department of Health and Human Services information related to payments and other transfers of value to physicians, other healthcare providers, and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members and applicable group purchasing organizations; and

- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws that may apply to items or services reimbursed by any third-party payor, including commercial insurers, state laws that require pharmaceutical companies to comply with the pharmaceutical industry s voluntary

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compliance guidelines and the relevant compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

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

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

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

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

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

failure by us to obtain and maintain regulatory approvals for the use of our products in various countries;

additional potentially relevant third-party patent rights;

complexities and difficulties in obtaining protection and enforcing our intellectual property;

difficulties in staffing and managing foreign operations;

complexities associated with managing multiple payor reimbursement regimes, government payors, or patient self-pay systems;

limits in our ability to penetrate international markets;

financial risks, such as longer payment cycles, difficulty collecting accounts receivable, the impact of local and regional financial crises on demand and payment for our products, and exposure to foreign currency exchange rate fluctuations;

natural disasters, political and economic instability, including wars, terrorism, and political unrest, outbreak of disease, boycotts, curtailment of trade, and other business restrictions;

certain expenses including, among others, expenses for travel, translation, and insurance; and

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regulatory and compliance risks that relate to maintaining accurate information and control over sales and activities that may fall within the purview of the U.S. Foreign Corrupt Practices Act, or FCPA, its books and records provisions, or its anti-bribery provisions.

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

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

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

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

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

Risks Related to this Offering and Ownership of Our Common Stock

The market price of our common stock may be highly volatile, and you may not be able to resell your shares at or above the initial public offering price.

Prior to this offering, there has not been a public market for our common stock. An active trading market for our common stock may not develop following this offering. You may not be able to sell your shares quickly or at

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the market price if trading in our common stock is not active. The initial public offering price for the shares has been determined by negotiations between us and the representative of the underwriters and may not be indicative of prices that will prevail in the trading market.

The market price of our common stock is likely to be volatile. Our stock price could be subject to wide fluctuations in response to a variety of factors, including but not limited to the following:

- adverse results or delays in preclinical or clinical studies;
- any inability to obtain additional funding;
- any delay in filing an IND, NDA, BLA, or other regulatory submission for any of our product candidates and any adverse development or perceived adverse development with respect to the applicable regulatory agency s review of that IND, NDA, BLA, or other regulatory submission;
- the perception of limited market sizes or pricing for our product candidates;
- failure to successfully develop and commercialize our product candidates;
- post-marketing safety issues;
- failure to maintain our existing strategic collaborations or enter into new collaborations;
- failure by us or our licensors and strategic collaboration partners to prosecute, maintain, or enforce our intellectual property rights;
- changes in laws or regulations applicable to our products;
- any inability to obtain adequate product supply for our product candidates or the inability to do so at acceptable prices;
- adverse regulatory decisions;
- introduction of new products, services, or technologies by our competitors;
- failure to meet or exceed financial projections we may provide to the public;
- failure to meet or exceed the financial projections of the investment community;

the perception of the pharmaceutical industry by the public, legislatures, regulators, and the investment community;

announcements of significant acquisitions, strategic partnerships, joint ventures, or capital commitments by us, our strategic collaboration partner, or our competitors;

disputes or other developments relating to proprietary rights, including patents, litigation matters, and our ability to obtain patent protection for our technologies;

additions or departures of key scientific or management personnel;

significant lawsuits, including patent or stockholder litigation;

if securities or industry analysts do not publish research or reports about our business, or if they issue an adverse or misleading opinion regarding our stock;

changes in the market valuations of similar companies;

general market or macroeconomic conditions;

sales of our common stock by us or our stockholders in the future; and

trading volume of our common stock.

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

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

As of January 10, 2014, our executive officers, directors, five percent stockholders, and their affiliates beneficially owned approximately 73% of our voting stock and, upon closing of this offering, that same group will beneficially own approximately 58% of our outstanding voting stock (assuming no exercise of the underwriters option to purchase additional shares and no exercise of outstanding options and warrants and no purchasing of shares by such persons in the directed share program). Therefore, even after this offering, these stockholders will have the ability to influence us through their ownership positions, which may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may believe are in your best interest as one of our stockholders.

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

We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in this prospectus and our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. We could be an emerging growth company for up to five years, although circumstances could cause us to lose that status earlier, including if the market value of our common stock held by non-affiliates exceeds $700.0 million as of any June 30 before that time or if we have total annual gross revenue of $1.0 billion or more during any fiscal year before that time, in which cases we would no longer be an emerging growth company as of the following December 31 or, if we issue more than $1.0 billion in non-convertible debt during any three-year period before that time, we would cease to be an emerging growth company immediately. We cannot predict if investors will find our common stock less attractive because we may rely on this exemption. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

If you purchase our common stock in this offering, you will incur immediate and substantial dilution in the book value of your shares.

Investors purchasing shares of common stock in this offering will pay a price per share that substantially exceeds the pro forma book value per share of our tangible assets after subtracting our liabilities and the preferred stock dividend that we will pay concurrent with this offering. As a result, investors purchasing shares of common stock in this offering will incur immediate dilution of $15.27 per share, based on an initial public offering price of $21.00 per share and our pro forma net tangible book value as of September 30, 2013. For information on how the foregoing amounts were calculated, see Dilution.

This dilution is due to the substantially lower price paid by our investors who purchased shares prior to this offering as compared to the price offered to the public in this offering, and the exercise of stock options granted to our employees. In addition, as of September 30, 2013, we had outstanding options and warrants to purchase 1,880,231 shares of our capital stock; the exercise of any of these options or warrants would result in additional dilution. As a result of the dilution to investors purchasing shares in this offering, investors may receive significantly less than the purchase price paid in this offering, if anything, in the event of our liquidation.

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

If our existing stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market after the lock-up and other legal restrictions on resale discussed in this prospectus lapse, the

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market price of our common stock could decline. Based upon the number of shares of common stock, on an as-converted basis, outstanding as of September 30, 2013, upon the closing of this offering we will have outstanding a total of 29,061,871 shares of common stock, assuming no exercise of the underwriters option to purchase additional shares. Of these shares, as of the date of this prospectus, approximately 5,760,369 shares of our common stock, plus any shares sold upon exercise of the underwriters option to purchase additional shares, will be freely tradable, without restriction, in the public market immediately following this offering, assuming that current stockholders do not purchase shares in this offering.

The lock-up agreements pertaining to this offering will expire 180 days from the date of this prospectus. After the lock-up agreements expire, based upon the number of shares of common stock, on an as-converted basis, outstanding as of September 30, 2013, up to an additional 23.3 million shares of common stock will be eligible for sale in the public market, of which approximately 17.0 million shares are held by directors, executive officers and other affiliates and will be subject to the manner of sale, volume limitations, and public reporting requirements of Rule 144 under the Securities Act of 1933, as amended, or the Securities Act. J.P. Morgan Securities LLC and Morgan Stanley & Co. LLC, however, may, in their sole discretion, permit our officers, directors, and other stockholders who are subject to these lock-up agreements to sell shares prior to the expiration of the lock-up agreements.

In addition, as of September 30, 2013, approximately 4.1 million shares of common stock that are either subject to outstanding options, reserved for future issuance under our equity incentive plans, or subject to outstanding warrants will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules, the lock-up agreements, and Rule 144 and Rule 701 under the Securities Act. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the market price of our common stock could decline.

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

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

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

Pursuant to our 2014 Incentive Plan, or the 2014 Plan, which will become effective immediately prior to the completion of this offering, our management is authorized to grant stock options and other equity-based awards to our employees, directors, and consultants. An aggregate of 2,250,000 shares will be available for issuance under the 2014 Plan. The number of shares available for future grant under the 2014 Plan will automatically increase on January 1 of each year by up to the least of 2,500,000 shares and 4% of all shares of our capital stock outstanding as of December 31 of the prior calendar year, subject to the ability of our compensation committee to take action to reduce the size of the increase in any given year. Currently, we plan to register the increased number of shares available for issuance under the 2014 Plan each year. Pursuant to our 2014 Employee Stock Purchase Plan, or 2014 ESPP, which will become effective immediately prior to the completion of this offering, eligible employees will be able to acquire shares of our common stock at a discount to the prevailing market price, and an aggregate of 600,000 shares will be available for issuance under the 2014 ESPP. The number of shares available for issuance under the 2014 ESPP will automatically increase on January 1 of each year by up to

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the least of 1,200,000 shares and 1% of all shares of our capital stock outstanding as of December 31 of the prior calendar year, subject to the ability of our compensation committee to take action to reduce the size of the increase in any given year. If our board of directors elects to increase the number of shares available for future grant under the 2014 Plan or the 2014 ESPP, our stockholders may experience additional dilution, which could cause our stock price to fall.

We have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

Our management will have broad discretion in the application of the net proceeds from this offering, including for any of the purposes described in the section entitled Use of proceeds, and you will not have the opportunity as part of your investment decision to assess whether the net proceeds are being used appropriately. Because of the number and variability of factors that will determine our use of the net proceeds from this offering, their ultimate use may vary from their currently intended use. The failure by our management to apply these funds effectively could harm our business. Pending their use, we may invest the net proceeds from this offering in investment-grade, interest-bearing securities. These investments may not yield a favorable return to our stockholders.

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

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

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

We have never declared or paid any cash dividends on our common stock. Although we will pay a cash dividend to our existing holders of preferred stock, which was agreed to at the time of the private placement financings, in connection with the consummation of this offering, we currently anticipate that we will retain future earnings for the development, operation, and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to stockholders will therefore be limited to the appreciation of their stock.

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

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

- authorize blank check preferred stock, which could be issued by our board of directors without stockholder approval and may contain voting, liquidation, dividend, and other rights superior to our common stock;

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create a classified board of directors whose members serve staggered three-year terms;

specify that special meetings of our stockholders can be called only by our board of directors or the chairperson of our board of directors;

prohibit stockholder action by written consent;

establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors;

provide that our directors may be removed only for cause;

provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum;

specify that no stockholder is permitted to cumulate votes at any election of directors;

expressly authorize our board of directors to modify, alter or repeal our amended and restated by-laws; and

require holders of 75% of our outstanding common stock to amend specified provisions of our amended and restated certificate of incorporation and amended and restated by-laws.

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

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

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

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements that involve risks and uncertainties. All statements other than statements of historical facts contained in this prospectus 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, se or the negative of these words or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- our expectations regarding the timing of reporting results from our clinical studies of rhGUS, triheptanoin and SA-ER;
- our expectations regarding the timing of commencing clinical studies with respect to KRN23, rhPPCA, and triheptanoin;
- the 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 expectations regarding the time during which we will be an emerging growth company under the JOBS Act;
- our expectations regarding the composition of our board of directors;
- our use of proceeds from this offering;

our financial performance; and

developments and projections relating to our competitors and our industry.

Any forward-looking statements in this prospectus 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 Risk Factors and elsewhere in this prospectus. 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 prospectus 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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USE OF PROCEEDS

We estimate that the net proceeds from the sale of 5,760,369 shares of common stock in this offering will be approximately $109.5 million at an initial public offering price of $21.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their option to purchase additional shares in full, we estimate that the net proceeds will be approximately $126.4 million after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

We are undertaking this offering in order to access the public capital markets and to increase our liquidity. As of September 30, 2013, we had cash, cash equivalents and marketable securities of approximately $63.7 million. We intend to use the net proceeds of this offering, together with our existing cash, cash equivalents and marketable securities, as follows:

- Approximately $9 million to advance our ongoing clinical program for KRN23, net of cost-share reimbursement from our partner KHK;
- Approximately $23 million to advance our ongoing clinical program for rhGUS;
- Approximately $41 million to advance our ongoing clinical program for triheptanoin in both LC-FAOD and Glut1 DS;
- Approximately $15 million to advance our ongoing clinical program for SA-ER;
- Approximately $4.3 million as a cash dividend to the holders of our preferred stock payable upon conversion of the preferred stock to common stock; and
- Although we have no plans to allocate specific amounts as of the date of this prospectus, the remainder for preclinical research, our ongoing clinical programs as described above, working capital, and other general corporate purposes.

Our expected use of net proceeds from this offering represents our current intentions based upon our present plans and business condition. As of the date of this prospectus, we cannot predict with complete certainty all of the particular uses for the net proceeds to be received upon the completion of this offering or the actual amounts that we will spend on the uses set forth above. We may also use a portion of the net proceeds to in-license, acquire, or invest in additional businesses, technologies, products, or assets. Although we have no specific agreements, commitments, or understandings with respect to any in-license or acquisition, we evaluate such opportunities and engage in related discussions with other companies from time to time. Due to the many variables inherent to the development of our product candidates, we cannot currently predict the stage of development we expect the net proceeds of this offering to achieve for our clinical studies and product candidates.

The amount and timing of our actual expenditures will depend upon numerous factors, including the results of our research and development efforts, the timing and success of preclinical studies, our ongoing clinical studies or clinical studies we may commence in the future and the timing of regulatory submissions. As a result, our management will have broad discretion over the use of the net proceeds from this offering.

Pending the use of the proceeds from this offering, we intend to invest the net proceeds in interest-bearing, investment-grade securities, certificates of deposit, or government securities.

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DIVIDEND POLICY

We have never declared or paid cash dividends on our common stock. Although we will pay a cash dividend to our existing holders of preferred stock, which was agreed to at the time of the private placement financings, in connection with the consummation of this offering, we currently intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business, and we do not anticipate paying any cash dividends on our common stock in the foreseeable future. Any future determination to pay dividends will be made at the discretion of our board of directors or any authorized committee thereof.

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CAPITALIZATION

The following table sets forth our cash, cash equivalents and marketable securities and capitalization as of September 30, 2013:

- on an actual basis;
- on a pro forma basis to reflect (i) the conversion of all outstanding shares of our convertible preferred stock into an aggregate of 19,598,486 shares of our common stock, (ii) the reclassification to additional paid-in capital of our preferred stock warrant liability in connection with the conversion of our outstanding preferred stock warrants into common stock warrants, and (iii) the accrual of a dividend of $4.3 million which is payable concurrent with the conversion of our preferred stock to common stock to the holders of our preferred stock, which has been calculated as if the conversion of preferred stock into common stock occurred as of January 30, 2014, in each case, immediately prior to the completion of this offering; and
- on a pro forma as adjusted basis to additionally reflect (i) the issuance and sale of 5,760,369 shares of common stock in this offering at an initial public offering price of $21.00 per share, after deducting the underwriting discount and commissions and estimated offering expenses payable by us and (ii) the payment of the $4.3 million dividend payable described above.

You should read this information together with our audited financial statements and related notes appearing elsewhere in this prospectus and the information set forth under the heading Selected Financial Data and Management s Discussion and Analysis of Financial Condition and Results of Operations.

	As of September 30, 2013		
	Actual	Pro Forma	Pro Forma as Adjusted
		(in thousands, except share and per share data) (unaudited)	
Cash, cash equivalents and marketable securities	$ 63,657	$ 63,657	$ 168,876
Preferred stock warrant liability	$ 1,596		
Convertible preferred stock, par value $0.001 per share: 62,459,236 shares authorized, 61,431,574 shares issued and outstanding, actual; no shares authorized, issued and outstanding, pro forma and pro forma as adjusted	118,002		
Stockholders deficit:			
Preferred stock, par value $0.001 per share: no shares authorized, issued or outstanding, actual; 25,000,000 shares authorized and no shares issued or outstanding, pro forma and pro forma as adjusted			
Common stock, par value $0.001 per share: 85,000,000 shares authorized, 3,703,016 shares issued and outstanding, actual; 250,000,000 shares authorized, 23,301,502 shares issued and outstanding pro forma, and 29,061,871 shares issued and outstanding, pro forma as adjusted	4	23	29
Additional paid-in capital	8	115,306	224,800
Accumulated other comprehensive loss	(14)	(14)	(14)
Deficit accumulated during the development stage	(56,846)	(56,846)	(56,846)
Total stockholders (deficit) equity	(56,848)	58,469	167,969
Total capitalization	$ 62,750	$ 58,469	$ 167,969

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The number of shares of common stock issued and outstanding in the table above excludes the following shares as of September 30, 2013:

- 1,526,772 shares of common stock issuable upon the exercise of outstanding stock options having a weighted-average exercise price of $0.86 per share;

- 353,459 shares of common stock issuable upon the exercise of outstanding warrants having a weighted-average exercise price $3.006 per share;

- 1,565,352 shares of common stock reserved for issuance pursuant to future equity awards under our 2011 Equity Incentive Plan, as amended, which will become available for issuance under our 2014 Incentive Plan after completion of this offering;

- 2,250,000 shares of common stock reserved for issuance (including the above-referenced shares reserved for issuance under our 2011 Equity Incentive Plan, as amended) pursuant to future equity awards under our 2014 Incentive Plan, as well as any future increases in the number of shares of our common stock reserved for future issuance under this plan, which will become effective immediately prior to the completion of this offering; and

- 600,000 shares of common stock reserved for future issuance under our 2014 Employee Stock Purchase Plan, or 2014 ESPP, as well as any future increases in the number of shares of our common stock reserved for future issuance under the 2014 ESPP, which will become effective immediately prior to the completion of this offering.

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DILUTION

If you invest in our common stock in this offering, your ownership interest will be diluted to the extent of the difference between the initial public offering price per share of our common stock and the pro forma as adjusted net tangible book value per share of our common stock immediately after this offering.

Net tangible book value per share is determined by dividing our total tangible assets less our total liabilities by the number of shares of common stock outstanding. Our historical net tangible book value as of September 30, 2013 was $(58.2) million, or $(15.72) per share. Our pro forma net tangible book value as of September 30, 2013 was $57.1 million, or $2.45 per share, based on the total number of shares of our common stock outstanding as of September 30, 2013. Pro forma net tangible book value, before the issuance and sale of shares in this offering, gives effect to:

- the conversion of all outstanding shares of our convertible preferred stock into an aggregate of 19,598,486 shares of our common stock;
- the reclassification to additional paid-in capital of our preferred stock warrant liability in connection with the conversion of our outstanding preferred stock warrants into common stock warrants; and
- a $4.3 million dividend payable concurrent with the conversion of the convertible preferred stock, which has been calculated as if the conversion of preferred stock into common stock occurred on January 30, 2014.

Dilution per share to new investors represents the difference between the amount per share paid by purchasers of shares of common stock in this offering and the pro forma as adjusted net tangible book value per share of common stock immediately after completion of this offering. After giving effect to our sale of shares of common stock in this offering at an initial public offering price of $21.00 per share, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, and the payment of the $4.3 million dividend payable, our pro forma as adjusted net tangible book value as of September 30, 2013 would have been $166.6 million, or $5.73 per share. This represents an immediate increase in pro forma net tangible book value of $3.28 per share to existing stockholders and an immediate dilution of $15.27 per share to investors participating in this offering, as illustrated in the following table:

Initial public offering price per share		$ 21.00
Historical net tangible book value per share as of September 30, 2013	$ (15.72)	
Pro forma increase in net tangible book value per share as of September 30, 2013	18.17	
Pro forma net tangible book value per share as of September 30, 2013	2.45	
Increase in pro forma net tangible book value per share attributable to new investors	3.28	
Pro forma as adjusted net tangible book value per share after this offering		5.73
Dilution per share to investors participating in this offering		$ 15.27

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If the underwriters option to purchase additional shares from us is exercised in full, the pro forma as adjusted net tangible book value per share after this offering would be $6.13 per share, the increase in pro forma net tangible book value per share to existing stockholders would be $3.68 per share and the dilution to investors participating in this offering would be $14.87 per share.

The following table presents, on a pro forma as adjusted basis described above, the differences between the existing stockholders and the purchasers of shares in this offering with respect to the number of shares purchased from us, the total consideration paid, which includes net proceeds received from the issuance of common and convertible preferred stock, cash received from the exercise of stock options and warrants, and the value of any stock issued for services and the average price paid per share (in thousands, except per share amounts and percentages):

	Shares Purchased		Total Consideration		Average Price per Share
	Number	Percent	Amount	Percent	
Existing stockholders	23,301,502	80%	$ 109,030	47%	$ 4.68
New investors	5,760,369	20	120,968	53	$ 21.00
Totals	29,061,871	100%	$ 229,998	100%	$ 7.91

The foregoing calculations exclude the following shares as of September 30, 2013:

- 1,526,772 shares of common stock issuable upon the exercise of outstanding stock options having a weighted-average exercise price of $0.86 per share;
- 353,459 shares of common stock issuable upon the exercise of outstanding warrants having a weighted-average exercise price of $3.006 per share;
- 1,565,352 shares of common stock reserved for issuance pursuant to future awards under our 2011 Equity Incentive Plan, as amended, which will become available for issuance under our 2014 Incentive Plan after completion of this offering;
- 2,250,000 shares of common stock reserved for issuance (including the above-referenced shares reserved for issuance under our 2011 Equity Incentive Plan, as amended) pursuant to future equity awards under our 2014 Equity Incentive Plan, as well as any future increases in the number of shares of our common stock reserved for future issuance under this plan, which will become effective immediately prior to the completion of this offering; and
- 600,000 shares of common stock reserved for future issuance under our 2014 Employee Stock Purchase Plan, or 2014 ESPP, as well as any future increases in the number of shares of our common stock reserved for future issuance under the 2014 ESPP, which will become effective immediately prior to the completion of this offering.

Furthermore, we may choose to raise additional capital through the sale of equity or convertible debt securities due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. New investors will experience further dilution if any of our outstanding options or warrants are exercised, new options are issued and exercised under our equity incentive plans or we issue additional shares of common stock, other equity securities or convertible debt securities in the future.

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SELECTED FINANCIAL DATA

The selected statements of operations data for the years ended December 31, 2011 and 2012 and the selected balance sheet data as of December 31, 2011 and 2012 are derived from our audited financial statements included elsewhere in this prospectus. The selected statements of operations data for the nine months ended September 30, 2012 and 2013 and the selected balance sheet data as of September 30, 2013 have been derived from our unaudited financial statements included elsewhere in this prospectus. The unaudited interim financial information has been prepared on the same basis as the annual financial information and, in the opinion of management, reflects all adjustments, which include only normal recurring adjustments, necessary to present fairly our financial position as of September 30, 2013 and the results of operations for the nine months ended September 30, 2012 and 2013. Our historical results are not necessarily indicative of the results that may be expected in the future and interim results are not necessarily indicative of results to be expected for the full year. You should read the selected historical financial data below in conjunction with the section titled Management s Discussion and Analysis of Financial Condition and Results of Operations and the financial statements and related notes included elsewhere in this prospectus.

	Year Ended December 31,		Nine Months Ended September 30,	
	2011	2012	2012	2013
	(in thousands, except share and per share amounts)		(unaudited)	
Statements of Operations Data:				
Operating expenses:				
Research and development	$ 4,717	$ 12,641	$ 8,866	$ 19,625
General and administrative	1,844	3,344	2,441	3,130
Total operating expenses	6,561	15,985	11,307	22,755
Loss from operations	(6,561)	(15,985)	(11,307)	(22,755)
Interest income	4	1		157
Interest expense	(270)			
Other expense	(22)	(350)	(97)	(1,155)
Net loss	$ (6,849)	$ (16,334)	$ (11,404)	$ (23,753)
Net loss attributable to common stockholders[1]	$ (7,466)	$ (19,561)	$ (12,749)	$ (31,624)
Net loss per share attributable to common stockholders, basic and diluted	$ (4.62)	$ (14.20)	$ (12.35)	$ (9.70)
Shares used to compute net loss per share attributable to common stockholders, basic and diluted	1,617,384	1,377,207	1,032,159	3,260,484
Pro forma net loss per share attributable to common stockholders, basic and diluted (unaudited)[1]		$ (2.04)		$ (1.17)
Shares used to compute pro forma net loss per share attributable to common stockholders, basic and diluted (unaudited)[1]		9,935,836		23,062,827

(1) See Notes 2 and 14 to our audited financial statements and Note 8 of our unaudited financial statements included elsewhere in this prospectus for an explanation of the calculations of basic and diluted net loss per share attributable to common stockholders and pro forma net loss per share attributable to common stockholders.

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	As of December 31,		As of September 30,
	2011	2012	2013
		(in thousands)	(unaudited)
Balance Sheet Data:			
Cash, cash equivalents and marketable securities	$ 10,645	$ 86,190	$ 63,657
Working capital	9,954	83,257	61,067
Total assets	12,129	88,316	68,592
Convertible preferred stock warrant liability	216	518	1,596
Convertible preferred stock	18,604	111,387	118,002
Deficit accumulated during the development stage	(8,155)	(27,058)	(56,846)
Total stockholders deficit	(7,961)	(27,047)	(56,848)

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

You should read the following discussion and analysis of our financial condition and results of operations together with the section of this prospectus entitled Selected Financial Data and our financial statements and related notes included elsewhere in this prospectus. This discussion and other parts of this prospectus contain forward-looking statements that involve risk and uncertainties, such as statements of our plans, objectives, expectations, and intentions. As a result of many factors, including those factors set forth in the Risk Factors section of this prospectus, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a development-stage biopharmaceutical company focused on the identification, acquisition, development, and commercialization of novel products for the treatment of rare and ultra-rare diseases, with an initial focus on serious, debilitating metabolic genetic diseases. We focus on diseases for which the unmet medical need is high, the biology for treatment is clear, and for which there are no approved therapies. Since our inception in 2010, we have in-licensed potential treatments for five different diseases that are or we expect will be in Phase 1/2 or Phase 2 clinical studies by early 2014. Our strategy, which is predicated upon time- and cost-efficient drug development, allows us to pursue multiple programs in parallel with the goal of delivering safe and effective therapies to patients with the utmost urgency.

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

Our biologics pipeline includes the following three product candidates:

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

- 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 initiated a Phase 1/2 clinical study in MPS 7 in December 2013.

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

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

- Triheptanoin, or UX007, is a synthetic oil with a specifically designed chemical composition being studied in an investigator-sponsored Phase 2 study for the treatment of long-chain fatty acid oxidation disorders, or LC-FAOD. This 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. We plan to initiate our own Phase 2 study in LC-FAOD in early 2014.

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Triheptanoin is also in an investigator-sponsored Phase 2 study for the treatment of glucose transporter type-1 deficiency syndrome, or Glut1 DS, a rare metabolic disease of brain energy deficiency that can result in seizures, developmental delay, and movement disorder. We plan to initiate our own Phase 2 clinical study in Glut1 DS in the first half of 2014.

SA-ER, or UX001, is an extended-release form of sialic acid in a Phase 2 study for the treatment of hereditary inclusion body myopathy, or HIBM, a neuromuscular disorder that causes muscle weakness and wasting. We reported 24-week data from our ongoing Phase 2 study in HIBM in July 2013 and reported top-line 48-week data in December 2013.

We are considered a development-stage company under U.S. generally accepted accounting principles, or U.S. GAAP, and have only a limited operating history. Since our inception in 2010, we have devoted substantially all of our resources to identify, acquire, and develop our product candidates, including conducting clinical studies and providing general and administrative support for these operations. We have funded our operations to date primarily from the issuance and sale of convertible preferred stock and convertible promissory notes.

We have never been profitable and have incurred net losses in each year since inception. Our net losses were $6.8 million and $16.3 million for the years ended December 31, 2011 and 2012, and $11.4 million and $23.8 million for the nine months ended September 30, 2012 and 2013. As of September 30, 2013 we had a deficit accumulated during the development stage of $56.8 million. Substantially all of our net losses have resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations.

Financial Operations Overview

Revenue

To date, we have not generated any revenue. We do not expect to receive any revenue from any product candidates that we develop until we obtain regulatory approval and commercialize our products 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.

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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 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, 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 marketable securities.

Interest expense

Interest expense consists of interest on outstanding borrowings under convertible promissory notes. We had no outstanding debt as of December 31, 2011 and thereafter as our convertible promissory notes and accrued interest were all converted into shares of Series A convertible preferred stock in 2011.

Other expense

Other expense primarily consists of gains and losses resulting from the remeasurement of our convertible preferred stock warrant liability. We will continue to record adjustments to the estimated fair value of the convertible preferred stock warrants until they are exercised, expired, or converted into warrants to purchase shares of our common stock upon the completion of a liquidity event, including the completion of an initial public offering. At that time, we will reclassify the convertible preferred stock warrant liability as 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. We

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believe that the accounting policies discussed below are critical to understanding our historical and future performance, as these policies relate to the more significant areas involving management s judgments and estimates.

Accrued Research and Development Expenses

As part of the process of preparing financial statements, we are required to estimate and accrue expenses, the largest of which is related to accrued research and development expenses. This process involves reviewing contracts and purchase orders, identifying services that have been performed on our behalf, and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual costs.

We record accruals for estimated costs of research, preclinical and clinical studies, and manufacturing development. These costs are a significant component of our research and development expenses. A substantial portion of our ongoing research and development activities is conducted by third-party service providers. We accrue the costs incurred under our agreements with these third parties based on actual work completed in accordance with agreements established with these third parties. We determine the actual costs through discussions with internal personnel and external service providers as to the progress or stage of completion of the services and the agreed-upon fee to be paid for such services. We make significant judgments and estimates in determining the accrual balance in each reporting period. As actual costs become known, we adjust our accruals. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and could result in us reporting amounts that are too high or too low in any particular period. Our accrual is dependent, in part, upon the receipt of timely and accurate reporting from clinical research organizations and other third-party vendors. To date, there have been no material differences from our accrued estimated expenses to the actual clinical trial expenses.

Estimated Fair Value of Convertible Preferred Stock Warrant Liability

Warrants for the purchase of Series A convertible preferred stock that are contingently redeemable are classified as liabilities on the balance sheet at their estimated fair value. At the end of each reporting period, changes in estimated fair value during the period are recorded in other expense, net. We will continue to adjust the carrying value of the warrants until the earlier of the exercise of the warrants or the completion of a liquidity event, including the completion of an initial public offering, at which time the liabilities will be reclassified to additional paid-in capital.

We estimate the fair values of our convertible preferred stock warrants using an option-pricing model based on inputs as of the valuation measurement dates, including our estimated equity value at the valuation measurement dates, the estimated volatility of the price of our convertible preferred stock, the remaining contractual terms of the warrants, and the risk-free interest rates.

Stock-Based Compensation

Stock-based compensation costs related to stock options granted to employees are measured at the date of grant based on the estimated fair value of the award, net of estimated forfeitures. We estimate the grant date fair value, and the resulting stock-based compensation expense, using the Black-Scholes option-pricing model. The grant date fair value of the stock-based awards is recognized on a straight-line basis over the requisite service period, which is generally the vesting period of the respective awards.

The Black-Scholes option-pricing model requires the use of highly subjective assumptions which determine the fair value of stock-based awards. These assumptions include:

Expected term The expected term represents the period that the stock-based awards are expected to be outstanding and is determined using the simplified method (based on the midpoint between the vesting date and the end of the contractual term).

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Expected volatility Since we are privately held and do not have any trading history for our common stock, the expected volatility was estimated based on the average volatility for comparable publicly traded biopharmaceutical companies over a period equal to the expected term of the stock option grants. When selecting comparable publicly traded biopharmaceutical companies on which we based our expected stock price volatility, we selected companies with comparable characteristics to us, including enterprise value, risk profiles, position within the industry, and with historical share price information sufficient to meet the expected life of the stock-based awards. The historical volatility data was computed using the daily closing prices for the selected companies shares during the equivalent period of the calculated expected term of the stock-based awards. We will continue to apply this process until a sufficient amount of historical information regarding the volatility of our own stock price becomes available.

Risk-free interest rate The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of option.

Expected dividend We have never paid dividends on our common stock and have no plans to pay dividends on our common stock. Therefore, we used an expected dividend yield of zero.

In addition to the assumptions used in the Black-Scholes option-pricing model, we must also estimate a forfeiture rate to calculate the stock-based compensation for our awards. We will continue to use judgment in evaluating the expected volatility, expected terms, and forfeiture rates utilized for our stock-based compensation calculations on a prospective basis.

For the years ended December 31, 2011 and 2012, stock-based compensation expense was $0.3 million and $0.9 million, respectively. For the nine month periods ended September 30, 2012 and 2013, stock-based compensation expense was $0.7 million and $0.4 million, respectively. As of September 30, 2013, we had $0.8 million of total unrecognized stock-based compensation costs, net of estimated forfeitures, which we expect to recognize over a weighted-average period of 2.4 years.

Fair Value of Common Stock

We are required to estimate the fair value of the common stock underlying our stock-based awards when performing the fair value calculations with the Black-Scholes option-pricing model. The fair value of the common stock underlying our stock-based awards was determined on each grant date by our board of directors, with input from management. Given the absence of a public trading market of our common stock, and in accordance with the American Institute of Certified Public Accountants, or AICPA, Practice Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*, our board of directors exercised reasonable judgment and considered numerous objective and subjective factors to estimate the fair value of our common stock.

All options to purchase shares of our common stock have been granted with an exercise price per share no less than the fair value per share of our common stock underlying those options on the date of grant. To assist our board of directors with the determination of the exercise price of our stock options and the fair value of the common stock underlying the options, we obtained third-party valuations of our common stock as of June 30, 2012, December 31, 2012, June 30, 2013, September 30, 2013, and November 30, 2013. Our board of directors considered the fair values of the common stock derived in the third-party valuations as one of the factors it considered when setting the exercise prices for options granted. Our board of directors also considered a range of objective and subjective factors and assumptions in estimating the fair value of our common stock on the date of grant, including:

progress of our research and development efforts;

our operating results and financial condition, including our levels of available capital resources;

rights and preferences of our common stock compared to the rights and preferences of our other outstanding equity securities;

our stages of development and material risks related to our business;

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the achievement of enterprise milestones, including entering into collaboration or license agreements and our progress in clinical trials;

the valuation of publicly-traded companies in the life sciences and biotechnology sectors, as well as recently completed mergers and acquisitions of peer companies;

equity market conditions affecting comparable public companies;

the likelihood of achieving a liquidity event for the shares of common stock, such as an initial public offering given prevailing market and biotechnology sector conditions; and

that the grants involved illiquid securities in a private company.

Contemporaneous Valuations

We obtained third-party valuations of our common stock as of June 30, 2012, December 31, 2012, June 30, 2013, and September 30, 2013 to assist our board of directors in estimating the fair value of our common stock at subsequent grant dates.

June 2012 and December 2012 Contemporaneous Valuations. The June 2012 and December 2012 valuations used the Back-Solve Method of the option-pricing method, or OPM, which derives the implied equity value for one type of equity security from a contemporaneous transaction involving another equity security. The June 2012 valuation, which was completed in July 2012, was based on the price of Series A convertible preferred stock that we sold to investors in July 2012. The December 2012 valuation was based on the price of Series B convertible preferred stock that we sold in December 2012. In both valuations, the contemporaneous transaction occurred in close proximity and involved third-party investors. Given the arm s-length nature of these financings, the close proximity of the Series A and Series B convertible preferred stock financings to the respective valuation dates, and the fair value hierarchy as described in FASB Accounting Standards Codification Topic 820, *Fair Value*, we believe the per share issuance prices of the Series A and Series B convertible preferred stock provide an indication of our equity value, as well as the fair value of common stock, as of June 30, 2012 and December 31, 2012, respectively.

The OPM treats common stock and preferred stock as call options on the total equity value of a company, with exercise prices based on the liquidation preference of the preferred stock. Under this method, the common stock has value only if the funds available for distribution to the stockholders exceed the value of the liquidation preference at the time of a liquidity event such as a merger, sale, or IPO, assuming the enterprise has funds available to make a liquidation preference meaningful and collectible by the stockholders. The common stock is modeled as a call option on the underlying equity value at a predetermined exercise price. In the model, the exercise price is based on a comparison with the total equity value, rather than, as in the case of a regular call option, a comparison with a per share stock price. The OPM uses the Black-Scholes option-pricing model to price the call option. This model defines the securities fair values as functions of the current fair value of a company and uses assumptions such as the anticipated timing of a potential liquidity event and the estimated volatility of the equity securities.

For purposes of the June 2012 valuation, we estimated the time to liquidity as 1.5 years based on then-current plans and estimates of our board of directors and management regarding a liquidity event. The volatility assumption was based on an analysis of guideline companies historical equity volatility factors for a period of 1.5 years, which is the term assumption. Based on this analysis of the guideline companies, a volatility assumption of 67% was selected and utilized. The risk-free rate was estimated as the interpolated 1.5 year U.S. Treasury yield. A discount for lack of marketability of 31% was then applied to the value indicated in our common stock. Based on these factors, the third party valuation concluded that our common stock had a fair value of $0.81 per share as of June 30, 2012.

For purposes of the December 2012 valuation, we estimated the time to liquidity as 2.0 years based on then-current plans and estimates of our board of directors and management regarding a liquidity event. The time to

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liquidity increased from 1.5 years from June 2012 to 2.0 years in December 2012 due to the completion of the Series B convertible preferred stock financing in December 2012, which provided us with the funds to be able to have a liquidity event at a later date. The volatility assumption was based on an analysis of guideline companies historical equity volatility factors for a period of 2.0 years, which is the term assumption. Based on this analysis of the guideline companies, a volatility assumption of 75% was selected and utilized. The risk-free rate was estimated as the interpolated 2.0 year U.S. Treasury yield. A discount for lack of marketability of 40% was then applied to the value indicated in our common stock. Based on these factors, the third-party valuation concluded that our common stock had a fair value of $1.82 per share as of December 31, 2012.

June 2013 Contemporaneous Valuation. For purposes of the June 2013 valuation, a hybrid method was used to determine our equity value, which is a hybrid between the probability-weighted return methodology, or PWERM, and the OPM. The PWERM is a scenario-based analysis that estimates the value per share based on the probability-weighted present value of expected future investment returns, considering each of the possible outcomes available to us, as well as the economic and control rights of each share class. In the hybrid method, the OPM is used to estimate the allocation of value within one or more of PWERM scenarios. The hybrid method can be a useful alternative to explicitly modeling all PWERM scenarios in situations when the company has transparency into one or more near-term exits but is unsure about what will occur if the current plans fall through. The hybrid model was selected at this time for the reasons described below relating to our plans for a potential IPO.

The OPM was used to allocate the equity value to the various securities under two scenarios. The first scenario assumed we would complete an IPO within 12 months and the second scenario assumed we would remain private beyond 12 months with a potential sale or merger in 2.0 years. The estimated time to liquidity was 1.0 year and 2.0 years based on timing of a liquidity event in the two scenarios. Based on an analysis of the guideline companies, a volatility assumption of 75% was selected and utilized for both scenarios. The risk-free rate was estimated based on the applicable U.S. Treasury yield. A discount for lack of marketability of 20% and 35% was applied to the value indicated in our common stock under the first scenario and the second scenario, respectively. As of June 30, 2013 our board of directors had not authorized our management to begin preparations for a potential IPO. The board made this decision in late July, and that is when we initiated our preparation process. The increased probability of an IPO was retroactively taken into consideration in the June 30, 2013 valuation, which is a critical factor contributing to the increase in the fair value of our common stock as of that date. Based on these factors, the third-party valuation concluded that our common stock had a fair value of $4.07 per share as of June 30, 2013.

September 2013 Contemporaneous Valuation. For purposes of the September 2013 valuation, a hybrid method was used to determine our equity value, which is consistent with the method used in the June 2013 valuation.

The OPM was used to allocate the equity value to the various securities under two scenarios. The first scenario assumed we would complete an IPO within six months and the second scenario assumed we would remain private beyond 12 months with a potential sale or merger in 1.5 years. We estimated a probability of 60% for the first scenario and 40% for the second scenario compared to a 50% weighting for each in the June 2013 valuation. The increase in the probability of an IPO was because, at the July 2013 meeting of our board of directors, preparations for a potential IPO were authorized, we subsequently selected a banking syndicate, and on September 6, 2013 an organizational meeting was held in order to begin the IPO process. The estimated time to liquidity was six months and 1.5 years based on timing of a liquidity event in the two scenarios. Based on an analysis of the guideline companies, a volatility assumption of 75% was selected and utilized for both scenarios. The risk-free rate was estimated based on the applicable U.S. Treasury yield. A discount for lack of marketability of 10% and 30% was applied to the value indicated in our common stock under the first scenario and the second scenario, respectively. In addition, in July 2013, we announced that we would initiate development of triheptanoin for a new indication, Glut1 DS, which was incorporated into the valuation. In August 2013, we entered into a collaboration agreement with KHK, which was also incorporated into the valuation. Based on these factors, the third-party valuation concluded that our common stock had a fair value of $6.86 per share as of September 30, 2013.

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November 2013 Contemporaneous Valuation. For purposes of the November 2013 valuation, a hybrid method was used to determine our equity value, which is consistent with the method used in the June 2013 and September 2013 valuations.

The OPM was used to allocate the equity value to the various securities under two scenarios. The first scenario assumed we would complete an IPO within three months and the second scenario assumed we would remain private beyond 12 months with a potential sale or merger in 1.5 years. We estimated a probability of 75% for the first scenario and 25% for the second scenario compared to 60% and 40%, respectively, in the September 2013 valuation. The increase in the probability of an IPO was due to the progress we have made since September 2013 in preparing for a potential IPO and in our development programs. In December 2013, we announced the dosing of the first patient in a Phase 1/2 study of rhGUS for MPS 7, our IND for triheptanoin for the treatment of Glut1 DS went into effect, and we released topline results from a 48-week Phase 2 clinical study of SA-ER showing apparent activity at the higher dose level. These developments were anticipated and taken into consideration in the November 2013 valuation. The estimated time to liquidity was three months and 1.5 years based on timing of a liquidity event in the two scenarios. Based on an analysis of the guideline companies, a volatility assumption of 70% was selected and utilized for both scenarios. The risk-free rate was estimated based on the applicable U.S. Treasury yield. A discount for lack of marketability of 5% and 30% was applied to the value indicated in our common stock under the first scenario and the second scenario, respectively. Based on these factors, the third-party valuation concluded that our common stock had a fair value of $11.19 per share as of November 30, 2013.

Stock Option Grants

Information regarding our stock option grants along with the estimated fair value per share of the underlying common stock, for stock options granted since January 1, 2012 is summarized in the table below:

Grant date	Number of common shares underlying options granted	Exercise price per common share	Estimated fair value per share of common stock
August 2, 2012	451,425	$ 0.81	$ 0.81
September 13, 2012	28,712	0.81	0.81
October 25, 2012	19,141	0.81	0.81
March 21, 2013	82,944	1.82	1.82
April 25, 2013	79,757	1.82	1.82
May 23, 2013	285,531	1.82	1.82
August 15, 2013	54,234	4.07	4.07
November 1, 2013	519,685	6.86	6.86
December 19, 2013	245,650	11.19	11.19

The intrinsic value of all outstanding options as of September 30, 2013 was $30.8 million based on the initial public offering price of $21.00 per share.

The estimated fair value per share of the common stock in the table above represents the determination by our board of directors of the fair value of our common stock as of the date of the grant, as discussed below.

Stock Options Granted in August, September, and October 2012. Our board of directors granted stock options on August 2, 2012, September 13, 2012, and October 25, 2012, each having an exercise price of $0.81 per share. In establishing this exercise price, our board of directors considered input from management, the results of our June 30, 2012 third-party valuation, the objective and subjective criteria discussed above as well as the following: (i) in September 2012, we obtained the rights to rhPPCA and in-licensed North American rights to triheptanoin; (ii) triheptanoin had primarily been studied in academic settings with data available only from uncontrolled clinical studies or in anecdotal form; and (iii) rhPPCA has only ever been studied in mice and *in*

vitro, and we have made very limited investments in the development of this compound to date. As each of these compounds was speculative, early stage, and would require significant funds and risk on our part to advance, our board of directors did not believe that these events increased our equity value.

In the judgment of our board of directors, there were no internal or external developments that would indicate that the fair value of our common stock would have increased from June 30, 2012. As a result, our board of directors concluded that the fair value of our common stock at each of these grant dates was $0.81 per share.

Stock Options Granted in March, April, and May 2013. Our board of directors granted stock options on March 21, 2013, April 25, 2013, and May 23, 2013, each having an exercise price of $1.82 per share. In establishing this exercise price, our board of directors considered input from management, the results of our December 31, 2012 third-party valuation, the objective and subjective criteria discussed above as well as the following: (i) a toxicology study for rhGUS, a retrospective study for triheptanoin, and the Phase 2 study for SA-ER were all ongoing during this time period, but no results had yet been generated; and (ii) these studies were all either underway or already contemplated at the time of the financing upon which the December 31, 2012 valuation was based. Given the lack of clarity around a future liquidity event, and the lack of any significant clinical data in the first five months of 2013, in the judgment of our board of directors, there were no internal or external developments that would indicate that the fair value of our common stock had increased from December 31, 2012. As a result, our board of directors concluded that the fair value of our common stock at each of these grant dates was $1.82 per share.

Stock Options Granted in August 2013. Our board of directors granted stock options on August 15, 2013, each having an exercise price of $4.07 per share. In establishing this exercise price, our board of directors considered input from management, the results of our June 30, 2013 third-party valuation, the objective and subjective criteria discussed above as well as the following: (i) the probability of an IPO was already taken into consideration in the June 30, 2013 valuation and there was no change in probability as of August 15, 2013; (ii) the interim analysis of the 24-week data in our study of SA-ER showed only modest efficacy; (iii) although we had announced development of triheptanoin for Glut1 DS between June 30, 2013 and August 15, 2013, no clinical development activity had yet commenced as of the latter date; and (iv) our acquisition of ex-U.S. rights to triheptanoin, which was announced in July 2013, was already taken into consideration in the valuation as of June 30, 2013. As a result, our board of directors concluded that the fair value of our common stock at this grant date was $4.07 per share.

Stock Options Granted in November 2013. Our board of directors granted stock options on November 1, 2013, each having an exercise price of $6.86 per share. In establishing this exercise price, our board of directors considered input from management, the results of our September 30, 2013 third-party valuation, and the objective and subjective criteria discussed above. The board of directors considered the increase in the probability of an IPO from 50% as of June 30, 2013 to 60% as of September 30, 2013 and also concluded that no further change in this probability had taken place as of November 1, 2013. In the judgment of our board of directors, there were no internal or external developments that would indicate the fair value of our common stock would have increased from September 30, 2013. As a result, our board of directors concluded that the fair value of our common stock at this grant date was $6.86 per share.

Stock Options Granted in December 2013. Our board of directors granted stock options on December 19, 2013, each having an exercise price of $11.19 per share. In establishing this exercise price, our board of directors considered input from management, the results of our November 30, 2013 third-party valuation, and the objective and subjective criteria discussed above. The board of directors considered the increase in the probability of an IPO from 60% as of September 30, 2013 to 75% as of November 30, 2013 and also determined that there were no internal or external developments that would indicate the fair value of our common stock would have increased from November 30, 2013, as all developments in December had been anticipated and taken into consideration at that date. As a result, our board of directors concluded that the fair value of our common stock at this grant date was $11.19 per share.

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Initial Public Offering Price

In consultation with the underwriters for this offering, we determined the initial public offering price for this offering. The initial public offering price is $21.00 per share. In comparison, our estimate of the fair value of our common stock was $11.19 per share as of November 30, 2013. We note that, as is typical in initial public offerings, the initial public offering price for this offering was not derived using a formal determination of fair value, but was determined by negotiation between us and the underwriters. Among the factors that were considered in setting this initial public offering price were the following:

- an analysis of the typical valuation ranges seen in recent initial public offerings for companies in our industry;
- the general condition of the securities markets and the recent market prices of, and the demand for, publicly traded common stock of generally comparable companies;
- an assumption that there would be a receptive public trading market for pre-commercial biotechnology companies such as us; and
- an assumption that there would be sufficient demand for our common stock to support an offering of the size contemplated by this prospectus.

The initial public offering price for this offering reflects an $9.81 increase over the estimated valuation as of November 30, 2013 of $11.19 per share. Investors should be aware of this difference and recognize that the initial public offering price for this offering is in excess of our prior valuations. Further, investors are cautioned not to place undue reliance on the valuation methodologies discussed above as an indicator of future stock prices. We believe the difference may be due to the following factors:

- The contemporaneous valuation prepared as of November 30, 2013 contained two liquidity scenarios, including an initial public offering to be completed within three months of November 30, 2013, to which we assigned a probability weighting of 75%. We also applied a discount for lack of marketability of 5% in the initial public offering scenario of our November 30, 2013 valuation, which discount is not applied when determining the initial public offering price for this offering. When the 5% discount for lack of marketability is not applied, the fair value per share of common stock in the initial public offering scenario as of November 30, 2013 would be $13.29.
- We also believe that continued progress in the development of our product candidates between December 19, 2013 (our most recent option grant date) and consummation of this offering accounts for part of the increase between the estimated value at November 30, 2013 and the initial public offering price for this offering. For example, we have further developed the clinical and regulatory strategy with respect to KRN23, and we have dosed our first patients in a Phase 1/2 study of rhGUS with no serious adverse events reported to date. We are also advancing our clinical programs for triheptanoin in both Glut1 DS and LC-FAOD, with enrollment expected to begin shortly in both trials. In addition, we have begun treating patients with higher doses of SA-ER with no serious adverse events reported to date.
- The initial public offering price necessarily assumes that this offering has occurred, a public market for our common stock has been created and that our preferred stock has converted into common stock in connection with this offering and, therefore, excludes the marketability or illiquidity discounts associated with the timing or likelihood of an initial public offering, the superior rights and preferences of our preferred stock and the alternative scenarios considered in the contemporaneous valuations over the past 18 months. Our November 30, 2013 valuation included an illiquidity discount of 5%.

In the public markets we believe there are investors who may apply more qualitative and subjective valuation criteria to certain of our clinical assets than the valuation methods applied in our valuations, although there can be no assurance that this will in fact be the case. As described above, as a private company we used a more quantitative methodology to determine the fair value of our common stock and this methodology differs from the methodology used to determine the initial public offering price for this offering. The initial public offering price for this offering was not derived using a formal determination of fair value, but rather was determined by negotiation between us and the underwriters.

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In particular, the estimate of fair value of our common stock as of November 30, 2013 was not a factor in setting the initial public offering price for this offering.

The price that investors are willing to pay in this offering may take into account other things that have not been expressly considered in our prior valuations, are not objectively determinable and that valuation models are not able to quantify.

Income Taxes

We use 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. We 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.

As of December 31, 2012, our total deferred tax assets were $10.1 million. Due to our lack of earnings history and uncertainties surrounding our ability to generate future taxable income, the net deferred tax assets have been fully offset by a valuation allowance. The deferred tax assets were primarily comprised of federal and state tax net operating losses and tax credit carryforwards. Utilization of the net operating loss and tax credit carryforwards may be subject to an annual limitation due to historical or future ownership percentage change rules provided by the Internal Review Code of 1986, and similar state provisions. The annual limitation may result in the expiration of certain net operating loss and tax credit carryforwards before their utilization.

Results of Operations

Comparison of the nine months ended September 30, 2012 and 2013

	Nine Months Ended September 30,		Dollar	%
	2012	2013	Change	Change
	(dollars in thousands)			
Operating expenses:				
Research and development	$ 8,866	$ 19,625	$ 10,759	121%
General and administrative	2,441	3,130	689	28%
Total operating expenses	11,307	22,755	11,448	101%
Loss from operations	(11,307)	(22,755)	(11,448)	101%
Interest income		157	157	*
Other expense	(97)	(1,155)	(1,058)	*
Net loss	$ (11,404)	$ (23,753)	$ (12,349)	108%

** not meaningful*

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Research and Development Expenses. Research and development expenses increased $10.8 million, or 121%, for the nine months ended September 30, 2013 compared to the same period in 2012. The following table summarizes our research and development expenses for the nine months ended September 30, 2012 and 2013 and for the period from April 22, 2010 (inception) through September 30, 2013.

	Nine Months Ended September 30,		Period from April 22, 2010 (Inception) Through September 30,
	2012	2013	2013
	(dollars in thousands)		
Development candidate:			
rhGUS	$ 1,903	$ 5,915	$ 9,561
rhPPCA	141	205	384
Triheptanoin (LC-FAOD)	281	4,074	4,620
Triheptanoin (Glut1 DS)		1,032	1,032
SA-ER	5,223	5,942	17,268
KRN23		124	124
Preclinical and other research costs	1,318	2,333	4,952
Total research and development expenses	$ 8,866	$ 19,625	$ 37,941

The increase in research and development expenses above is primarily due to:

- for rhGUS, an increase of $4.0 million related to the development and manufacturing associated with supplying the product candidate for our toxicology and clinical studies;
- for triheptanoin (LC-FAOD), an increase of $3.8 million related to the initiation of our program in 2013, which included $0.8 million we paid to exercise the option with Baylor Research Institute, or BRI, pursuant to our license agreement with BRI to license the rights to triheptanoin in all territories outside of North America and $1.0 million in personnel-related costs as we allocated resources to this program, and costs related to the manufacture of clinical supplies;
- for triheptanoin (Glut1 DS), an increase of $1.0 million related to costs associated with the start up of clinical activities, including $0.4 million in personnel costs as we allocated resources to this program;
- for SA-ER, an increase of $0.7 million related to the increase in clinical activities for this program; and
- an increase of $1.0 million in preclinical and other product development costs for various other potential product candidates.

General and Administrative Expenses. General and administrative expenses increased $0.7 million, or 28%, for the nine months ended September 30, 2013 compared to the same period in 2012. The increase in general and administrative expenses was primarily due to increases in professional services costs and in personnel costs in support of our research and development activities.

Interest Income. Interest income increased $0.2 million for the nine months ended September 30, 2013 compared to the same period in 2012, primarily due to funds invested from our Series B convertible stock financing completed in December 2012.

Other Expense. Other expense increased $1.1 million for the nine months ended September 30, 2013 compared to the same period in 2012. The increase was due to the fair value remeasurement of the liability related to our convertible preferred stock warrants.

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Comparison of Years Ended December 31, 2011 and 2012

	Year ended December 31,		Dollar	%
	2011	2012	Change	Change
	(dollars in thousands)			
Operating expenses:				
Research and development	$ 4,717	$ 12,641	$ 7,924	168%
General and administrative	1,844	3,344	1,500	81%
Total operating expenses	6,561	15,985	9,424	144%
Loss from operations	(6,561)	(15,985)	(9,424)	144%
Interest income	4	1	(3)	*
Interest expense	(270)		270	*
Other expense	(22)	(350)	(328)	*
Net loss	$ (6,849)	$ (16,334)	$ 9,485	138%

* *not meaningful*

Research and Development Expenses. Research and development expenses increased $7.9 million, or 168%, for the year ended December 31, 2012 compared to the same period in 2011. The following table summarizes our research and development expenses for the years ended December 31, 2011 and 2012 and for the period from April 22, 2010 (inception) through September 30, 2013.

	Year Ended December 31,		Period from April 22, 2010 (Inception) through
	2011	2012	December 31, 2012
	(in thousands)		
Development candidate:			
rhGUS	$ 438	$ 3,198	$ 3,646
rhPPCA	7	172	179
Triheptanoin (LC-FAOD)		546	546
SA-ER	3,570	6,840	11,326
Preclinical and other research costs	702	1,885	2,619
Total research and development expenses	$ 4,717	$ 12,641	$ 18,316

The increase in research and development expenses above is primarily due to:

- for SA-ER, an increase of $3.3 million related to the development and manufacturing costs for our various clinical studies, increase in personnel costs, and the costs for our Phase 2 clinical study;

for rhGUS, an increase of $2.8 million related to the development and manufacturing costs associated with supplying rhGUS for our various clinical studies;

for triheptanoin, an increase of $0.5 million related to the increase in clinical activities, as well as $0.3 million paid to BRI to license the rights to triheptanoin; and

an increase of $1.2 million in preclinical and other research costs for various other potential product candidates.

General and Administrative Expenses. General and administrative expenses increased $1.5 million, or 81%, for the year ended December 31, 2012 compared to the same period in 2011. The increase in general and administrative expenses was primarily due to increases in professional services costs and in personnel costs in support of our research and development activities.

Interest Expense. Interest expense decreased $0.3 million for the year ended December 31, 2012 compared to the same period in 2011. The decrease is due to the conversion of the outstanding convertible promissory notes and related accrued interest into shares of our Series A convertible preferred stock in June 2011.

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Other Expense. Other expense increased $0.3 million for the year ended December 31, 2012 compared to the same period in 2011. The increase was primarily due to the fair value remeasurement of the liability related to our convertible preferred stock warrants.

Liquidity and Capital Resources

Since our inception, we have funded our operations primarily with $103.9 million in net proceeds from the sale of convertible preferred stock and $3.6 million in proceeds received from convertible promissory notes. As of September 30, 2013, we had $63.7 million in cash, cash equivalents, and marketable securities and a deficit accumulated during the development stage of $56.8 million.

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

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

	Year Ended December 31,		Nine Months Ended September 30,	
	2011	2012	2012	2013
			(unaudited)	
Cash used in operating activities	$ (5,825)	$ (12,504)	$ (8,790)	$ (21,427)
Cash used in investing activities	(924)	(1,191)	(1,067)	(58,847)
Cash provided by financing activities	17,329	89,240	15,228	133
Net increase (decrease) in cash and cash equivalents	$ 10,580	$ 75,545	$ 5,371	$ (80,141)

Cash Used in Operating Activities

Cash used in operating activities for the nine months ended September 30, 2013 was $21.4 million and reflected net loss of $23.8 million, offset by non-cash charges of $0.3 million for depreciation and amortization, $1.0 million for the amortization of premium paid on purchased marketable securities, $0.4 million for stock-based compensation and $1.1 million for the revaluation of convertible preferred stock warrant liability. Cash used in operating activities also reflected a $2.7 million increase in prepaid expenses and other current assets primarily due to deferred offering costs related to our IPO and an increase in interest income receivable as our invested funds increased with the sale of our Series B convertible preferred stock in December 2012. The increase was offset by a $2.4 million increase in accounts payable and accrued liabilities primarily due to higher clinical study and related costs as we continued to increase our research and development activities.

Cash used in operating activities for the nine months ended September 30, 2012 was $8.8 million and reflected net loss of $11.4 million, offset by non-cash charges of $0.2 million for depreciation and amortization, $0.7 million for stock-based compensation and $0.1 million for the revaluation of convertible preferred stock warrant liability. Cash used in operating activities reflected an increase of $1.6 million in accounts payable and accrued liabilities related to higher clinical study and related costs and other research and development activities.

Cash used in operating activities for the year ended December 31, 2012 was $12.5 million and reflected net loss of $16.3 million, offset by non-cash charges of $0.9 million for stock-based compensation, $0.3 million for depreciation and amortization, and $0.3 million expense for the revaluation of the convertible preferred stock warrant liability. Cash used in operating activities also reflected an increase in accounts payable and accrued and other liabilities of $2.4 million related to higher clinical study and related costs and other research and development activities.

Cash used in operating activities for the year ended December 31, 2011 was $5.8 million and reflected net loss of $6.8 million, offset by non-cash charges of $0.3 million for interest expense related to the convertible promissory notes and $0.3 million for stock-based compensation. Cash used in operating activities also reflected

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an increase in accounts payable and accrued and other liabilities of $0.7 million as we continued to increase our research and development activities and the timing of payments made to our vendors, which was partially offset by an increase in prepaid expenses and other current assets of $0.2 million.

Cash Used in Investing Activities

Cash used in investing activities for the nine months ended September 30, 2013 was $58.8 million and related to purchases of marketable securities of $63.1 million, proceeds from maturities of marketable securities of $4.5 million and purchases of property and equipment of $0.3 million.

Cash used in investing activities for the nine months ended September 30, 2012 was $1.1 million and primarily related to purchases of property and equipment related to our move to a new leased facility in March 2012.

Cash used in investing activities for the year ended December 31, 2012 was $1.2 million and related to purchases of property and equipment of $1.1 million related to our move to a new leased facility in March 2012 and an increase in restricted cash of $0.1 million.

Cash used in investing activities for the year ended December 31, 2011 was $0.9 million and was related to purchases of property and equipment of $0.5 million and an increase in restricted cash of $0.4 million.

Cash Flows Provided by Financing Activities

Cash provided by financing activities for the nine months ended September 30, 2013 was $0.1 million related to proceeds from the issuance of common stock for the exercise of stock options.

Cash provided by financing activities for the nine months ended September 30, 2012 was $15.2 million and primarily related to net proceeds from the issuance of convertible preferred stock of $15.1 million.

Cash provided by financing activities for the year ended December 31, 2012 was $89.2 million and primarily related to net proceeds from the issuance of convertible preferred stock of $89.0 million.

Cash provided by financing activities for the year ended December 31, 2011 was $17.3 million and related to net proceeds from the issuance of $14.9 million of convertible preferred stock and $2.4 million of promissory notes.

Funding Requirements

We believe that our existing capital resources, not including the proceeds we receive from this offering, will be sufficient to meet our projected operating requirements for at least the next 12 months. We anticipate that we will continue to generate losses for the foreseeable future, and we expect the losses to increase as we continue the development of, and seek regulatory approvals for, our product candidates, and begin to commercialize any approved products. If we need to raise additional capital to fund our operations and complete our ongoing and planned clinical studies, funding may not be available to us on acceptable terms, or at all. We expect to finance future cash needs through public or private equity or debt offerings. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may be required to delay, limit, reduce, or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

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

- the scope, rate of progress, results and cost of our clinical studies, nonclinical testing, and other related activities;
- the cost of manufacturing clinical supplies, and establishing commercial supplies, of our product candidates and any products that we may develop;

the number and characteristics of product candidates that we pursue;

the cost, timing, and outcomes of regulatory approvals;

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the cost and timing of establishing sales, marketing, and distribution capabilities; and

the terms and timing of any collaborative, licensing, and other arrangements that we may establish, including any required milestone and royalty payments thereunder.

Contractual Obligations

The following table summarizes our contractual obligations at December 31, 2012 (in thousands):

	Payments due by period				
	Less than 1 year	1 to 3 years	3 to 5 years	More than 5 years	Total
Operating leases	$ 345	$ 570	$ 332	$	$ 1,247

JOBS Act Accounting Election

The Jumpstart our Business Startups Act of 2012, or the JOBS Act, permits an emerging growth company such as us to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies. We are choosing to opt out of this provision and, as a result, we will comply with new or revised accounting standards as required when they are adopted. This decision to opt out of the extended transition period under the JOBS Act is irrevocable.

Newly Adopted Accounting Pronouncements

In February 2013, the Financial Accounting Standards Board issued Accounting Standards Update No. 2013-02, or ASU 2013-02, Reporting of Amounts Reclassified Out of Accumulated Other Comprehensive Income. ASU 2013-02 requires reporting and disclosure about changes in accumulated other comprehensive income balances and reclassifications out of accumulated other comprehensive income. We adopted this guidance as of January 1, 2013 on a prospective basis, and this adoption did not have an impact on our financial statements.

Off-Balance Sheet Arrangements

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

Quantitative and Qualitative Disclosures About Market Risk

Our exposure to market risk for changes in interest rates relates primarily to interest earned on our cash equivalents and marketable securities. The primary objective of our investment activities is to preserve our capital to fund operations. A secondary objective is to maximize income from our investments without assuming significant risk. Our investment policy provides for investments in low-risk, investment-grade debt instruments. As of September 30, 2013, we had cash, cash equivalents, and marketable securities totaling $63.7 million consisting of bank deposits, money market funds, and investment-grade corporate bonds which are subject to default, changes in credit rating, and changes in market value. The securities in our investment portfolio are classified as available for sale and are subject to interest rate risk and will decrease in value if market interest rates increase. A hypothetical 10% change in interest rates during any of the period presented would not have had a material impact on our financial statements. To date, we have not experienced a loss of principal on any of our investments.

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

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BUSINESS

Overview

We are a development-stage biopharmaceutical company focused on the identification, acquisition, development, and commercialization of novel products for the treatment of rare and ultra-rare diseases, with an initial focus on serious, debilitating metabolic genetic diseases. We focus on diseases for which the unmet medical need is high, the biology for treatment is clear, and for which there are no approved therapies. Since our inception in 2010, we have in-licensed potential treatments for five different diseases that are or we expect will be in Phase 1/2 or Phase 2 clinical studies by early 2014. Our strategy, which is predicated upon time- and cost-efficient drug development, allows us to pursue multiple programs in parallel with the goal of delivering safe and effective therapies to patients with the utmost urgency.

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

- KRN23, or UX023, is an antibody targeting fibroblast growth factor 23, or FGF23, intended for the treatment of X-linked hypophosphatemia, or XLH, a rare genetic disease that impairs bone growth. We are developing KRN23 pursuant to our collaboration with Kyowa Hakko Kirin Co., Ltd., or KHK. KHK has conducted one Phase 1 study, one Phase 1/2 study and one Phase 1/2 extension study of KRN23 in adults with XLH. Data from the Phase 1/2 studies should be available in 2014. We expect to continue the clinical development of KRN23 in adults as well as initiate pediatric clinical development in 2014.

- 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 initiated a Phase 1/2 clinical study in MPS 7 in December 2013.

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

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

- Triheptanoin, or UX007, is a synthetic oil with a specifically designed chemical composition being studied in an investigator-sponsored Phase 2 study for the treatment of long-chain fatty acid oxidation disorders, or LC-FAOD. This 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. We plan to initiate our own Phase 2 study in LC-FAOD in early 2014.

- Triheptanoin is also in an investigator-sponsored Phase 2 study for the treatment of glucose transporter type-1 deficiency syndrome, or Glut1 DS, a rare metabolic disease of brain energy deficiency that can result in seizures, developmental delay, and movement disorder. We plan to initiate our own Phase 2 clinical study in Glut1 DS in the first half of 2014.

- SA-ER, or UX001, is an extended-release form of sialic acid in a Phase 2 study for the treatment of hereditary inclusion body myopathy, or HIBM, a neuromuscular disorder that causes muscle weakness and wasting. We reported 24-week data from our ongoing Phase 2 study in HIBM in July 2013 and reported top-line 48-week data in December 2013.

Our current product candidate pipeline has been either in-licensed from academic institutions or derived from partnerships with other pharmaceutical companies. Where possible, our strategy is to acquire and retain

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global commercialization rights to our products to maximize long-term value. Over time, we intend to build our own commercial organization, which we believe will be of modest size due to the relatively small number of specialists who treat patients with rare and ultra-rare diseases.

The patients we seek to treat have diseases with limited or no treatment options, and we recognize that their lives and well-being are highly dependent upon our efforts to develop new therapies. For this reason, we are passionate about developing these therapies with the utmost urgency and care. We strive to build a company that is faster, better, and smarter about advancing multiple product candidates through approval.

We were founded in April 2010 by our current President and Chief Executive Officer, Dr. Emil Kakkis, M.D., Ph.D., who is the former Chief Medical Officer of BioMarin Pharmaceutical Inc. We have assembled an experienced team with extensive drug development and commercialization capabilities, particularly in the orphan drug area. Dr. Kakkis and the team at Ultragenyx have been previously involved at other companies, in the development and/or commercialization of many therapies approved or in development for rare metabolic genetic diseases, including Aldurazyme, Naglazyme, Kuvan, and Vimizim (BioMarin); Lumizyme/Myozyme (Sanofi-Genzyme); and asfotase alpha (Enobia; now Alexion). Our investors include, but are not limited to, the following entities or their affiliates or funds advised by them: TPG Biotech, Fidelity Biosciences (Beacon Bioventures), HealthCap, Pappas Ventures, Adage Capital Partners, L.P., Capital Research Global Investors, Columbia Wanger Asset Management, Jennison Associates LLC, BlackRock, Inc., Genzyme Corporation, Shire LLC, and Ramius LLC.

Our Strategy

Our strategy is to identify, acquire, develop, and commercialize novel products for the treatment of rare and ultra-rare diseases in the United States, the European Union, and select international markets, with the goal of becoming a leading rare disease biotechnology company. The critical components of our business strategy include the following:

Focus on rare and ultra-rare diseases with significant unmet medical need. There are numerous rare and ultra-rare metabolic genetic diseases that currently have no approved drug therapy and for which no therapies are currently in development. Patients suffering from these diseases often have a high unmet medical need with significant morbidity and/or mortality. We are focused on developing and commercializing therapies for multiple such indications with the utmost urgency.

Focus on diseases and therapies with clear mechanisms of action. We also focus on diseases that have biology and root causes that are well understood. For example, several of our product candidates are replacement therapies for a single deficient enzyme or substrate in the body. We believe that developing drugs that directly impact known disease pathways will increase the probability of success of our development programs.

Leverage our experience and relationships to in-license promising product candidates. Our management team has strong relationships with key opinion leaders in the metabolic genetic field, as well as a history of success in the development and commercialization of therapies for rare and ultra-rare genetic diseases. Accordingly, we enjoy unique access to many in-licensing opportunities. All of our current product candidates are in-licensed from academic institutions or derived from partnerships with other pharmaceutical companies on attractive terms. We believe these parties have agreed to license product candidates to us because they are confident in our drug development capabilities and experience in bringing rare disease therapies to market.

Develop and commercialize multiple product candidates in parallel. Clinical studies for rare and ultra-rare diseases can often be smaller, fewer in number, and less expensive than those for larger market indications. Development of multiple programs in the metabolic genetics field also generates organizational efficiencies and economies of scale. As a result of these efficiencies, we can feasibly develop multiple clinical-stage product candidates in parallel, resulting in a more diversified portfolio that provides multiple opportunities to create value.

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Focus on excellent and rapid clinical and regulatory execution. We believe that building a successful and sustainable rare disease-focused company requires very specific expertise in the areas of patient identification, clinical study design and conduct, and regulatory strategy. We have assembled a team with a successful track record in managing global clinical development activities in an efficient manner, and with multinational experience in obtaining regulatory approvals for rare disease products.

Seek to retain global commercialization rights to product candidates. We intend to seek and retain global commercialization rights to our product candidates whenever possible to maximize the potential value of our product portfolio. Our plan is to establish our own commercial organization in major pharmaceutical markets and develop a network of third-party distributors in smaller markets. We believe this commercial organization can be modest and targeted due to the relatively small number of specialists who typically treat patients with the diseases to be addressed by our product candidates. As a result, we do not expect that we will require pharmaceutical partners for commercialization of our product candidates, although we may consider partnering for certain territories or indications or for other strategic purposes.

Product Candidates

The following table summarizes our product candidate pipeline:

Biologics product candidates

KRN23 (UX023) for the treatment of XLH

KRN23 is a fully human monoclonal antibody administered via subcutaneous injection that is designed to bind and reduce the biological activity of FGF23 to increase abnormally low phosphate levels in patients with XLH. In August 2013, we formed a collaboration with and licensed certain intellectual property from Kyowa Hakko Kirin Co., Ltd., or KHK, to jointly develop and commercialize KRN23 for the treatment of XLH. KHK has conducted one Phase 1 study, one Phase 1/2 study and one Phase 1/2 extension study of KRN23 in adults with XLH. We reviewed data from the Phase 1/2 studies prior to entering into our collaboration with KHK, and we expect to release data for the Phase 1/2 studies in 2014. We expect to continue the clinical development of KRN23 in adults as well as initiate pediatric clinical development in 2014.

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XLH disease background

Patients with XLH have low serum phosphate, which can also be referred to as phosphorous, 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. FGF23 is produced by cells responsible for bone formation to manage calcification as part of bone growth and remodeling by signaling to the kidney to promote phosphate excretion and to suppress vitamin D production when phosphate levels are too high. Low phosphate levels lead to poor bone mineralization and a variety of clinical manifestations, including skeletal deformity, bone pain, short stature, gross motor impairment, muscle weakness, and lower than normal bone density. XLH is an inherited genetic disease that can be genetically confirmed and affects both males and females. Diagnosis of the disease typically takes place via assessment of clinical presentation, x-ray of the bones, and urine and blood tests to confirm renal phosphate wasting.

XLH patients have a genetic deficiency in a regulatory system that senses phosphate levels and uses FGF23 to control serum phosphate. The deficiency interferes with this regulatory process and leads to abnormal up-regulation of FGF23, which causes phosphate wasting by the kidney. FGF23 induces profound reductions in serum phosphate levels by two mechanisms simultaneously: reducing renal reabsorption via reducing expression of a sodium phosphate co-transporter, as well as reducing intestinal phosphate reabsorption via a reduction in active vitamin D production.

There is no approved drug therapy or treatment for the underlying cause of XLH. Most patients are managed using oral phosphate replacement and vitamin D therapy, which is only partially effective at restoring bone physiology and growth and has significant side effects. These therapies require extremely close monitoring due to the potential for excessive spikes in phosphate levels, which can result in severe damage to the kidneys from excess calcium and 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. We believe XLH patients need a better treatment option that is more specific to the underlying cause of the disease and safer in how it manages phosphate levels.

KRN23 background and clinical development

KRN23 is designed to bind FGF23 and interfere with a required co-stimulatory signaling mechanism. The interference in FGF23 signaling is intended to prevent phosphate wasting in the urine and increase serum phosphate levels. Increased serum phosphate levels are intended to improve bone mineralization and reduce the severity of the clinical manifestations of XLH.

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The following graphic illustrates the pathophysiology of XLH and the mechanism of action of KRN23.

KHK has conducted one Phase 1 study, one Phase1/2 study, and one Phase 1/2 extension 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 in October 2013 and demonstrated that KRN23 was well tolerated and increased serum phosphate, or phosphate in the blood, and vitamin D levels. Of the 38 adult XLH patients, 12 received a single subcutaneous injection of KRN23 (at doses of 0.1, 0.3, 0.6, or 1.0 mg/kg), 17 received a single intravenous injection of KRN23 (at doses of 0.003, 0.01, 0.03, 0.1, or 0.3 mg/kg) and 9 received placebo. The effect of KRN23 on the increase in serum phosphate levels was comparable between intravenous and subcutaneous administration; however, time to reach peak effect was slower and duration of effect was greater with subcutaneous administration compared with intravenous administration. Although the phosphate levels did not reach the normal range, the demonstrated improvement suggests that significant benefit could be expected. No serious adverse events were reported in the Phase 1 study, although some patients (approximately 82%) experienced non-serious treatment-emergent adverse events. The most common non-serious treatment-emergent adverse events in the study overall were nausea and headache, although no patients in the placebo or subcutaneous treatment arms reported these events. In the subcutaneous arm, two patients (approximately 17%) experienced elevated levels of the enzyme amylase in the blood, and two patients (approximately 17%) experienced back pain. There did not appear to be a relationship between the incidence and types of adverse events and the dose administered following a single dose of study drug. The following graphics illustrate the results of KHK s Phase 1 single dose study relating to serum phosphate and vitamin D levels after subcutaneous injection, which is the route of administration planned for use in all subsequent clinical trials. Increases were statistically significant at the 0.3, 0.6, and 1.0 mg/kg

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subcutaneous dose levels, with p-values less than 0.05 for serum phosphate and less than 0.001 for vitamin D. P-values are an indication of statistical significance reflecting the probability of an observation occurring due to chance alone. Differences with a p-value of less than 0.05 are considered statistically significant.

Serum Phosphate (mg/dL)

Vitamin D (pg/mL)

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

Potential market opportunity

Based on incidence and prevalence rates published in a Danish epidemiologic study and surveys of physicians in the United States, we estimate that there are approximately 3,000 cases of XLH in pediatric patients in the United States. Further, there are an estimated 9,000 cases of XLH in adult patients in the United States. However, we expect that many of these adult patients may not seek treatment if their bone disease is not too severe.

rhGUS (UX003) for the treatment of MPS 7

We are developing recombinant human beta-glucuronidase, or rhGUS, as an intravenous, or IV, enzyme replacement therapy for the treatment of MPS 7, also known as Sly Syndrome. Patients with MPS 7 suffer from severe cellular and organ dysfunction that typically leads to death in the teens or early adulthood. MPS 7 is caused by a deficiency of the lysosomal enzyme beta-glucuronidase, or GUS, 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. We licensed exclusive worldwide rights to rhGUS-related know-how and cell lines from Saint Louis University in November 2010. We initiated a Phase 1/2 study of rhGUS in MPS 7 patients in December 2013 and expect to report interim data in 2014.

MPS 7 disease background

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. Significant enlargement of the liver and spleen and an abnormal ribcage, when combined with frequent recurrent and chronic infections, can lead to progressive respiratory compromise and failure. Heart disease is also common in patients with severe MPS 7, although it may not develop or manifest until later in life. Lysosomal storage of GAGs within the joint tissues can lead to significant stiffness and restriction of mobility in the hip, shoulder, elbow, and knee joints. All of these disease complications can result in severe pain or the inability to walk. Additional symptoms can include corneal clouding, hernias, visual loss, hearing loss, and developmental delay.

Most MPS 7 patients die between their teenage years and thirties, though some may live longer. The most severe form of the disease can uniquely present at birth with non-immune hydrops fetalis, which is fatal in the majority of affected patients and may account for as much as half of the disease incidence. Non-immune hydrops fetalis is a very severe neonatal condition in which the child retains an enormous amount of fluid throughout the body. Infants with hydrops fetalis rarely survive beyond a few weeks to a few months of age.

MPS 7 is often suspected from coarsened facial features, physical disease, and liver enlargement on clinical examination. Urine tests demonstrate excess GAG excretion, and the specific MPS disease is definitively diagnosed through tests that demonstrate a deficiency in GUS enzyme activity. Prenatal diagnostic tools have also been used to verify if a fetus has a deficiency of the enzyme and is affected with the disease.

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There are currently no approved drug therapies for MPS 7. A few patients have been given bone marrow or hematopoetic stem cell transplants, but their skeletal and connective tissue disease is not effectively treated by these transplants, and the morbidity and mortality of the transplant procedure can be significant, particularly if not conducted during the first two years of life.

rhGUS background

GUS is an enzyme found in the lysosome, a digestive compartment inside the cell needed to process sugars, fats, and proteins. As with other lysosomal enzymes, uptake of GUS into cells and tissues occurs by a particular receptor that recognizes a certain residue on the enzyme, known as mannose-6-phosphate, which is critical for optimal tissue distribution and rapid clearance of GAGs. Studies in cell culture and *in vivo* have demonstrated that our rhGUS product candidate is taken up into cells efficiently by this receptor, resulting in the delivery of the enzyme into the lysosomes and clearance of stored GAGs in MPS 7 animal models. The following graphic illustrates the receptor-mediated uptake of the rhGUS enzyme by the diseased cell and the subsequent clearance of storage of accumulated GAGs in the lysosomes.

The use of enzyme replacement therapy as a potential treatment is based on 20 years of research work in murine models of the disease. Historical studies in preclinical models of MPS 7 have shown that human or mouse GUS enzyme replacement achieves distribution to many tissues, including the brain, and significantly reduces or prevents lysosomal storage during treatment. The reduced lysosomal storage correlates with significant improvements in bone development, growth, cognitive ability, hearing, immune function, and survival.

Efficacy data from randomized controlled Phase 3 studies conducted by third parties for other enzyme deficiencies treated with other enzyme replacement therapies have been published for other related lysosomal diseases, including MPS 1, MPS 6, and MPS 2. All three of these enzyme replacement therapies reduced lysosomal storage in Phase 3 clinical studies resulting in reduction in liver size to normal or near normal, as well as significant reduction in spleen size. Additionally, the three enzyme replacement therapies showed improvement in pulmonary function, walking ability, joint range of motion in patients with more severe joint mobility restriction, and sleep apnea for those patients with abnormal airway function during sleep at baseline. Urinary GAG excretion also decreased significantly in these studies. All three products have been approved in the United States and the European Union as well as other territories worldwide based on safety and efficacy presented in these Phase 3 programs. Based on these results, we believe there is a strong rationale for our approach to treat MPS 7 with rhGUS.

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Preclinical results

We have conducted preclinical studies to support the chronic intravenous, or 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 was noted in these studies. The following graph shows dose-dependent urinary GAG reduction in mice after administration of rhGUS for eight weeks.

For the toxicology program, rhGUS was administered in two species, with no infusion-associated reactions or clinical problems noted.

Clinical development

In December 2013, we initiated an open-label, Phase 1/2 study to evaluate the safety, tolerability, efficacy, and dose of IV administration every other week of rhGUS in four to five patients with MPS 7 who are between five and 30 years of age. The initial 12-week treatment period will be followed by a dose-titration period and a long-term extension study. We expect to receive interim data from this study in 2014. If results from the initial 12-week treatment period from this study are supportive, we plan to initiate a pivotal Phase 3 study enrolling at least 12 patients.

With respect to our rhGUS program, although we have not yet filed an investigational new drug, or IND, application, we have held meetings regarding the pathway for potential approval of the program for MPS 7 with the United States Food and Drug Administration, or the FDA, and the European Medicines Agency, or EMA. The EMA agreed that approval under exceptional circumstances could be possible for a proposed 12-patient placebo-controlled pivotal study in this disease with urinary GAG levels as a surrogate primary endpoint provided the data was strongly supportive of a favorable benefit/risk ratio. The EMA requested that some evidence or trend in improvement in clinical endpoints be observed to support the primary endpoint, but recognized that a statistically significant result on clinical endpoints was unlikely given the small number of patients expected to be enrolled in the study. The FDA would like to see additional data correlating urinary GAG levels with other clinical endpoints, which we plan to collect both through our Phase 1/2 study as well as through an ongoing retrospective study correlating urinary GAG levels with clinical endpoints in other MPS diseases.

In addition to the above development plan, we intend to study MPS 7 patients under the age of five years, including younger infants born with hydrops fetalis. Currently, these infants often die within a few months to one

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year, but enzyme replacement therapy might be able to reduce GAG storage and improve health and survival in these patients. We are also supplying rhGUS to an investigator who is treating a single U.S. patient under an emergency IND. We expect that results from the treatment of this patient will be presented at the Lysosomal Disease Network s 10th Annual World Symposium in February of 2014.

Potential market opportunity

Through our ongoing survey work with metabolic clinics, we have identified approximately 90 potential MPS 7 patients worldwide to date, including approximately 15 in the United States. Based on our experiences with other MPS diseases, we expect that, over time, more patients will be identified during patient identification efforts globally, potentially resulting in up to approximately 200 patients in the developed world. Based on published literature, we also estimate that approximately 20 patients per year worldwide are born with non-immune hydrops fetalis due to MPS 7. The establishment of efficacy and safety with our therapy may help drive ascertainment of MPS 7 patients.

rhPPCA (UX004) for the treatment of galactosialidosis

We licensed the rights to recombinant human protective protein cathepsin-A, or rhPPCA, from St. Jude Children s Research Hospital in September 2012. rhPPCA 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. As with MPS 7, an enzyme deficiency results in accumulation of substrates in the lysosomes, causing skeletal and organ dysfunction, and death. In galactosialidosis, the missing protease, cathepsin A, is a lysosomal stabilizing agent for the two other enzymes: sialidase and beta-galactosidase. Cathepsin A is therefore also called protective protein, or PPCA. PPCA enzyme deficiency leads to an accumulation of oligosaccharides, or short sugar chains. Enzyme replacement therapy *in vitro* and in the mouse model of this condition has shown that the replacement of PPCA results in reduction in storage of oligosaccharides in multiple organs, just as has been observed in other enzyme replacement therapies. In the 2014 to 2015 timeframe, we intend to pursue process development and manufacture development-scale quantities of rhPPCA in order to conduct proof-of-concept experiments in preclinical animal models of galactosialidosis. Depending on the results of our proof-of-concept preclinical studies, we may begin clinical studies in 2015 or 2016.

Small-molecule product candidates

Triheptanoin (UX007) for the treatment of LC-FAOD

We are developing triheptanoin for oral liquid administration intended as a substrate replacement therapy for patients with long-chain fatty acid oxidation disorders, or LC-FAOD. Patients with LC-FAOD have a deficiency that impairs both fatty acid metabolism and the Krebs cycle, which is a series of chemical reactions inside the body s cells that generate energy from fat. Triheptanoin is a medium-chain triglyceride of three seven-carbon fatty acids designed to provide substrate replacement for both fatty acid metabolism and the Krebs cycle and restore production of energy. We have exclusively in-licensed global rights to triheptanoin from Baylor Research Institute. Triheptanoin is in an ongoing investigator-sponsored Phase 2 study, and we plan to initiate a Phase 2 study in LC-FAOD patients in early 2014.

LC-FAOD background

Without sufficient fatty acid oxidation and Krebs cycle function, LC-FAOD patients cannot rely on fatty acids for energy as would normally occur, making such patients more reliant on glucose metabolism and more susceptible to severe energy crises during periods of fasting and illness. The inability to produce energy from fat can lead to depletion of all glucose in the body, and severe liver, muscle, and heart disease. These symptoms can lead to serious hospitalizations or early death. Due to altered energy balance in skeletal muscle, many patients experience low muscle tone, weakness, exercise intolerance, muscle pain and fatigue, low-grade chronic rhabdomyolysis (muscle rupture), and severe acute episodes of rhabdomyolysis requiring hospitalization. As LC-FAOD is a known cause of sudden infant death syndrome, patients born with all types of LC-FAOD in the

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United States are now diagnosed via newborn screening in all 50 states. Outside of the United States, patients are increasingly diagnosed by newborn screening, though they can also be diagnosed as a result of symptomatic presentations such as serious liver, muscle, and heart disease.

Patients with LC-FAOD have defects in genes that code for multiple enzymes involved in converting long chains of fat into energy. LC-FAOD patients are also thought to become deficient in the intermediate compounds that are required for the normal metabolic function of the Krebs cycle. This deficiency may be caused by damage to the mitochondria due to the accumulation of long-chain fatty acids, or due to the consumption of the intermediates in the production of glucose to overcome low blood glucose levels.

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-chain triglyceride, or MCT, oil supplementation. MCT oil has medium even-chain fatty acids that can be metabolized by medium-chain fatty acid oxidation enzymes and can bypass long-chain fatty acid oxidation enzyme blocks, but does not provide odd-chain fatty acids that can refill the Krebs cycle or be converted to new glucose. In many patients, the current standard of care, including MCT oil, does not prevent all hypoglycemic events, exercise intolerance, muscle weakness, rhabdomyolysis, and cardiomyopathy, as well as associated mortality. For example, a mortality rate of more than 50% has been observed in spite of treatment with standard of care. Major metabolic decompensations also persist despite newborn screening.

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Triheptanoin background and clinical development

Triheptanoin consists of medium-length odd-chain fatty acids that should bypass blocks in the long-chain fatty acid oxidation pathway and also restore function of the Krebs cycle. Triheptanoin is converted into heptanoate and ketone bodies; once these metabolites enter the mitochondria, they are metabolized by the medium-chain oxidation enzymes, bypassing the defective long-chain enzymes. These metabolites are converted into two-carbon units (pathway 1 in the figure below) and three-carbon units (pathway 2 in the figure below) required to fuel and operate the Krebs cycle. With these two substrates entering the Krebs cycle, the energy production process can continue and generate the adenosine triphosphate, or ATP, used to support cellular metabolism.

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Triheptanoin has been studied by academic researchers for over a decade in a large cohort of human FAOD subjects. Multiple investigator-sponsored open-label studies suggest clinical improvements with triheptanoin treatment, even for patients who were on standard of care. In 2006, a cumulative summary was reported for 48 FAOD subjects who were initially on standard of care but were then treated with triheptanoin, demonstrating a large decrease in liver enlargement and low blood sugar in nearly all subjects, a substantial decrease in frequency of muscle rupture, and a decrease in cardiac disease. Below is a chart summarizing the data reported in the 2006 study.

Triheptanoin has been studied clinically for 13 years in approximately 130 human subjects affected by a variety of diseases, including 65 patients with LC-FAOD. Over this 13-year period, six deaths have been reported among the LC-FAOD patients, but none of these were considered by investigators to be related to triheptanoin. Triheptanoin has been generally well tolerated when administered to subjects with all subtypes of LC-FAOD. Some patients have had non-serious treatment-emergent adverse events involving the gastrointestinal, or GI, system, such as cramping, diarrhea, and loose stools. These GI side effects can be managed by slowly increasing the dose when initiating therapy and by mixing triheptanoin with food or drink, but some patients have discontinued therapy due to the GI upset. In addition, excess weight gain has been reported and can be prevented with careful monitoring of total caloric intake.

The serious adverse events reported for the 65 subjects generally involved events consistent with the underlying LC-FAOD disease, including muscle weakness or pain, myoglobinuria, or muscle protein in the urine, muscle cell rupture, metabolic crisis, cardiomyopathy, hypoglycemia and elevated creatine kinase, or CK, often in association with infections, exercise, or during periods of limited triheptanoin treatment. Other serious adverse events involved events such as infections, fever and vomiting from unspecified cause, respiratory distress/breathing problems, falling oxygen saturation rate, seizure, or medical procedures apparently unrelated to FAOD such as reaction to injection, cleft palate repair, ear tube placement, tonsillectomy/adenoidectomy, cardiac stent placement.

Only three serious adverse events (6%) were classified as possibly related to triheptanoin treatment: muscle cell rupture and elevated CK reported for two subjects, and myoglobinuria in conjunction with exercise, suboptimal triheptanoin dose, and no fluid intake reported for one subject. All three of these serious adverse events were reported during treatment with low dose triheptanoin, and these serious adverse events can be considered typical of the underlying disease.

We have completed a retrospective medical record review study to assess the clinical outcome of triheptanoin treatment on LC-FAOD subjects who have been participating in a compassionate use program at the University of Pittsburgh Medical Center. The data were presented at the 12th International Conference of Inborn Errors of Metabolism in September 2013. The study evaluated the impact of triheptanoin treatment on the rate and extent of hospitalizations in 20 of 24 patients who have been treated with triheptanoin for up to 13 years as part of compassionate use and who consented to be part of the study. The study involved an intensive medical

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record collection and review of patients to capture major medical events available, during the period before and after initiation of treatment until the present time. A total of 120 individual charts were evaluated, which covered 241 years of patient data and included a total of 319 hospitalizations. The study compared the major medical event rate before and after initiation of triheptanoin treatment including the total number of hospitalizations and hospital days per year due to all causes, muscle rupture, hypoglycemia, or cardiomyopathy. The total number of events or hospital days for each patient was divided by the total number of years pre-treatment or post-treatment initiation to calculate an annual rate. The preliminary results of our retrospective medical record review are as follows:

(1) Excludes data for four infants dosed within first six months of life.

(2) Excludes hospitalizations with unknown discharge dates.

(3) Four infants were dosed within the first six months of life.

(4) Includes only those patients with hypoglycemia events prior to treatment.

(5) Includes only those patients with rhabdomyolysis events prior to treatment.

We have conducted a pre-investigational new drug, or pre-IND, meeting with the FDA and agreed on the immediate non-clinical and clinical development plan. Accordingly, we can proceed with our clinical program in patients aged six months and older. An IND is in effect, which allows us to commence human clinical studies.

In early 2014, we plan to initiate a prospective open-label Phase 2 study of triheptanoin treatment in approximately 30 severely affected LC-FAOD subjects exhibiting significant clinical symptoms despite current therapy. The study will be conducted at approximately eight clinical sites in the United States and Europe. Subjects will continue current therapy for four weeks to establish their baseline condition and then begin treatment with triheptanoin. We anticipate that dosing will be gradually increased to an effective dose, expected to be 25-35% of total caloric intake, while ensuring tolerability. The subjects will be followed over 24 weeks, then may continue treatment for an additional 54 weeks. The effects of treatment on clinical and physiologic disease will be assessed in three areas: skeletal myopathy, liver disease, and cardiac disease. A principal goal of the study is to determine the appropriate clinical endpoints and patient populations for testing in potential later-stage pivotal studies.

In addition to advancing our own development program toward potential approval, we are supporting multiple compassionate use and independent investigator-sponsored clinical studies in FAOD and other indications.

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Potential market opportunity

Based upon data from the National Newborn Screening Information System, we estimate that there are approximately 2,000 to 3,500 LC-FAOD patients in the United States, depending on the assumed mortality rate. It is unclear how many of these patients are currently diagnosed because the availability of newborn screening in all 50 states in the United States is a relatively new development. Furthermore, until further clinical development of triheptanoin is conducted, it is not clear which subsets of diagnosed patients would be considered by clinicians to be good candidates for triheptanoin treatment. Outside of the United States, where newborn screening is not consistently done, figures regarding the prevalence of LC-FAOD are more uncertain. To further understand the patient population, we have begun a survey of individual metabolic clinics, and to date we have individually identified over 1,300 LC-FAOD patients worldwide, including over 600 in the United States.

Triheptanoin (UX007) for the treatment of Glut1 DS

We are also developing triheptanoin 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 blood into the brain. Because glucose is the primary source of energy for the brain, Glut1 DS results in a chronic state of energy deficiency in the brain. Triheptanoin in this indication is intended as a substrate replacement therapy to provide an alternative source of energy to the brain in Glut1 DS patients. We plan to initiate an adaptive 52-week Phase 2 study in Glut1 DS patients in the first half of 2014, in which the study enrollment may be adapted based on an interim analysis of efficacy and seizure reduction data. The primary efficacy objective of the study is the reduction in frequency of generalized or partial-onset seizures compared to placebo. If the magnitude of benefit is substantial, the study enrollment may increase, whereas if it is not, then the target enrollment will remain the same.

Glut1 DS background

Glut1 DS is characterized by seizures, developmental delay, and movement disorder in approximately 90%, 75%, and 90% of patients, respectively. The seizures experienced by patients with Glut1 DS can be of many types, and more than one type of seizure can occur in the same patient. In infants and young children, the phenotype is dominated by the seizure disorder and developmental delay. The majority of children with Glut1 DS experience problems with language, both in speaking and in understanding what is said to them. In older patients and in some less severe patients, motor dysfunction has been the dominant symptom.

Patients are suspected of having Glut1 DS based on clinical grounds and a low cerebrospinal fluid, or CSF, glucose level. The diagnosis can be confirmed using a red cell glucose uptake test, but this test is not universally available. Currently, genetic testing is readily available and constitutes the main diagnostic test in suspected cases.

There are currently no approved drugs specific to Glut1 DS. Patients may be treated with antiepileptic drugs, or AEDs, for seizure control, although the seizures of Glut1 DS are generally considered resistant to existing AEDs. 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. The ketogenic diet is effective in controlling or reducing the seizures of Glut1 DS in most cases. However, seizures are not controlled completely in all patients on the ketogenic diet, and many patients have difficulties fully complying with the diet. Some patients continue to have significant problems with developmental delay and motor dysfunction despite improvement in seizures. We believe that a treatment that does not require an extreme diet therapy could help reduce the burden of Glut1 DS and potentially improve the developmental and other outcomes, without the adverse effects of the diet.

Triheptanoin background and clinical development

The rationale for using triheptanoin as a therapeutic treatment for Glut1 DS is that triheptanoin is a specially designed synthetic triglyceride compound intended to provide patients with heptanoate; heptanoate can circulate and also be further metabolized to four- and five-carbon ketone bodies in the liver. These metabolites bypass the

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Glut1 transporter to cross the blood-brain-barrier and provide an alternative energy source to the brain. Heptanoate also crosses the blood-brain-barrier and can be converted to glucose. As in LC-FAOD, some of these metabolites have the ability to restore proper functioning of the Krebs cycle within the brain. The following illustrates the mechanism of action of triheptanoin in the treatment of Glut1 DS.

There are a number of third-party publications on triheptanoin that provide data on its efficacy in epilepsy models and its absorption and metabolism when administered intravenously and orally at doses up to 40% of recommended daily caloric intake.

To date, there are no reports of toxicity on triheptanoin when used as an alternate source of energy in the diet. The metabolites of triheptanoin are essential as a source of energy in patients with Glut1 DS. They are therefore not expected to be toxic. Two toxicity studies have been reported in the literature; toxicities were not observed in either study, other than increased liver fat, which may have been related to high fat intake.

Triheptanoin has been studied clinically for 13 years in approximately 130 human subjects affected by a variety of diseases. Of these, 51 subjects were pediatric subjects with some as young as neonates, and 23 of the 51 pediatric subjects received over five years of treatment with triheptanoin. These data support the safety of triheptanoin when administered at approximately 35% of daily caloric intake in pediatric patients. Although an open-label investigator-sponsored clinical study is ongoing and the results have not yet been reported, there are anecdotal reports of benefit in terms of reduced seizures and improved development rate in some Glut1 DS subjects taking triheptanoin.

We are planning to initiate a clinical development program to study the effects of triheptanoin in Glut1 DS. We anticipate that the program will initially consist of a Phase 2 adaptive, randomized, double-blind, placebo-controlled, parallel-group study of at least 30 patients between three and 17 years of age inclusive who are currently not on, or not fully compliant with, ketogenic diet. Enrolled subjects will be allowed to maintain standard of care treatment with up to three AEDs and will record their generalized or partial-onset seizure frequency during the baseline period. At the end of the baseline period, eligible subjects will be randomized to either placebo or triheptanoin and will gradually increase their dose to approximately 35% of total daily calories. Subjects will then maintain a stable dose of study drug for six weeks. When 30 subjects have completed the treatment period, an independent data monitoring committee will review the efficacy and seizure reduction data to consider modifying the target patient enrollment. After the initial double-blind treatment period, the open-label extension period will begin, wherein all subjects will be treated with triheptanoin through week 52 of the study. The study will evaluate the impact of treatment with triheptanoin on seizure frequency, cognitive and other developmental delay, and movement disorder/motor abnormalities, as well as safety and tolerability. We expect to initiate this study in the first half of 2014.

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Potential market opportunity

While a comprehensive genetic analysis of birth incidence has not been conducted, published literature suggests a range of 3,000 to 7,000 Glut1 DS patients in the United States based on evaluations of generalized or absence seizures. The increasing recognition of alternative or variable motor forms of the disease suggests that older patients may be discovered over time. Given that the disease can be inherited as an autosomal dominant disease, the discovery of one patient may be used to identify other affected relatives in some cases, which can be important in marketing of the product.

Our clinic survey in Glut1 DS has only recently begun. To date, we have identified over 200 individual patients worldwide, including more than 80 in the United States, and we continue to contact clinics and expand the survey.

SA-ER (UX001) for the treatment of HIBM

We are developing an extended-release, oral formulation of sialic acid, or SA-ER, for the treatment of HIBM, which is also known as GNE myopathy. Sialic acid is an essential, naturally occurring amino sugar found in humans and most organisms. SA-ER is intended as a substrate replacement therapy designed to address sialic acid deficiency and restore muscle function in HIBM patients. We are the licensee or owner of patents and patent applications relating to sialic acid and its use for HIBM. SA-ER has completed a Phase 2 clinical study and we released top-line results in December 2013. We expect to continue to evaluate SA-ER in the extension portion of the Phase 2 study during 2014 and expect data from the extension portion of the study will be available in late 2014.

HIBM background

HIBM can be genetically confirmed and 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. In HIBM patients, distal motor function in the legs is first affected by muscle weakness and atrophy but nearly all muscles become progressively weaker, leading to patients becoming wheelchair bound within ten to twenty years from onset. Although all muscles in HIBM patients are generally affected to some degree, the quadriceps and certain facial and diaphragm muscles may be relatively spared from severe disease. Diagnosis of HIBM typically takes place via assessment of clinical presentation and muscle biopsy.

Patients with HIBM have a genetic defect in the gene coding for a particular enzyme. The enzyme is involved in the first step in the biosynthesis of sialic acid, which is required for the glycosylation of proteins and lipids. Therefore, patients with these mutations typically have a sialic acid deficiency. Sialic acid is needed for many proteins and lipids in the body for normal function. In patients with HIBM, a partial deficiency of this enzyme leads to a sialic acid deficiency in the muscle, which interferes with muscle function, leading to myopathy and atrophy.

There is no approved drug therapy for HIBM. Patients typically become wheelchair-bound within ten to 20 years from onset.

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SA-ER background and clinical development

SA-ER is designed to replace deficient sialic acid in HIBM patients. The underlying pathophysiology of HIBM has been subject to some debate, whereby it has been hypothesized that the deficient enzyme may have functions other than sialic acid biosynthesis. However, no alternative functions have been definitively established, and subsequent studies have shown that sialic acid substrate replacement in mouse models has profound beneficial effects on the phenotype with little residual clinical disease or pathology remaining after treatment. Therefore, we believe that sialic acid biosynthesis is a key function of the deficient enzyme, and we do not anticipate that theories regarding other functions of the deficient enzyme will impact our SA-ER development program. The following graphic illustrates the biosynthetic pathway of sialic acid in the body.

We have conducted a Phase 1 single-dose and repeat-dose safety and pharmacokinetics study of SA-ER in 26 HIBM patients at doses up to six grams per day. No serious adverse events were reported in the study, and adverse events were considered mild to moderate. SA-ER was absorbed and provided steady and significant drug levels over a period of 8 16 hours, depending on the dose level, regardless of inter-patient variability in the degree of absorption. At the six-gram per day repeat dose, taking SA-ER with food seemed to extend the time period in terms of elevated drug levels. At higher dose levels, mean sialic acid concentrations reached levels that were two to three times normal sialic acid levels.

We have conducted a Phase 2 randomized, double-blind, placebo-controlled study testing SA-ER for safety, pharmacodynamics and efficacy in 46 HIBM patients. The primary objective of the Phase 2 study was to evaluate safety, dose, and potential pharmacodynamic effect of restoring sialylation of muscle in patients with a confirmed genetic mutation for HIBM. The study also evaluated clinical measures of muscle strength, mobility, function, self-reported disability, and changes in quality of life. Patients were randomized to receive placebo, 3 grams, or 6 grams per day of SA-ER. At 24 weeks, placebo patients were randomized and crossed over into either of the two dose groups on a blinded basis and followed for an additional 24 weeks.

An interim analysis of the Phase 2 study was performed following 24 weeks of treatment. The data showed modest dose-dependent improvement in muscle strength compared to declines in placebo-treated subjects in some muscle groups, particularly in the upper extremities at the 6-gram dose. Similar to the results observed at the 24-week interim analysis, at 48 weeks the comparison of the upper extremity composite of muscle strength for the combined group of patients on 6 grams showed a modest increase and a statistically significant difference relative to the decline in strength observed in the combined groups on 3 grams. In the 6-gram cohort treated for 48 weeks, the modest increase in upper extremity strength observed at 24 weeks was sustained relative to a further decline in the comparable 3-gram group. These changes were more pronounced in those patients that have less advanced disease as assessed by a greater walking ability at baseline, a predefined subset. The lower

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extremity composite did not show a statistically significant difference between the dose groups, but neither group showed a significant decline during the treatment period. The upper extremity and lower extremity composites are predefined endpoints that aggregate change in muscle strength across multiple individually measured muscle groups.

The GNE Myopathy Functional Activity Scale, a patient-reported outcome measure developed to assess the clinical meaningfulness of changes in function, showed a trend toward a positive effect in the combined 6-gram group as compared to the combined 3-gram group. The sit-to-stand test also showed a trend toward a positive effect. Other clinical endpoints related to walking, including the six-minute walk test did not reveal significant changes in function, upward or downward. SA-ER appeared to be well tolerated with no serious adverse events observed to date in either dose group. Most adverse events were mild to moderate and most commonly gastrointestinal. A detailed presentation or publication of the 24- and 48-week data is expected in 2014. Following the 48-week analysis, we plan to continue to treat these patients in an extension study with an increased dosage of 12 grams based on the dose dependence observed at weeks 24 and 48. All 46 patients from the original study have elected to continue into the extension study, and approximately 10 new treatment-naïve patients will also be enrolled. Patients will receive 6 grams of SA-ER tablets plus 6 grams of an immediate-release capsule formulation of sialic acid per day. We anticipate that data from the extension study should be available in late 2014. We are also pursuing development of preclinical prodrugs of sialic acid, which may have better absorption into muscle tissue.

We have also initiated a disease monitoring program that is intended to improve the body of knowledge about HIBM and its typical course. This program is being conducted in partnership with the University of Newcastle s TREAT-NMD organization, a global neuromuscular physician network in Newcastle, England. The program is designed to integrate an online registry capturing patient-reported information, a fully monitored physician-driven natural history study, and potentially any post-approval patient follow-up into a single cohesive program.

Potential market opportunity

Approximately 400 HIBM cases have been reported in the published literature. HIBM is expected to occur in one in every 1,600 persons of Persian Jewish descent. Patients have also been identified in Asian Indian, European, Chinese, Japanese, Korean, and Middle Eastern populations. To better understand the patient population, we conducted an initial survey of 420 myopathy clinics in the United States, and the extrapolated results suggest a patient population of 300 to 400 in the United States and 1,200 to 2,000 worldwide. Our recent patient identification efforts have resulted in over 300 HIBM patients in the United States to date, and over 800 worldwide.

Competition

The commercialization of new drugs is competitive, and we may face worldwide competition from individual investigators, major pharmaceutical companies, specialty pharmaceutical companies, biotechnology companies, nutraceutical companies, and ultimately biosimilar and generic companies. Our competitors may develop or market therapies that are more effective, safer, or less costly than any that may be commercialized by us, or may obtain regulatory approval for their therapies more rapidly than we may obtain approval for ours.

The acquisition or licensing of pharmaceutical products is also very competitive, and a number of more established companies, which have acknowledged strategies to license or acquire products, may have competitive advantages as may other emerging companies taking similar or different approaches to product acquisitions. These established companies may have a competitive advantage over us due to their size, cash flows, and institutional experience.

With respect to KRN23, although we are not aware of any other products currently in clinical development for the treatment of XLH, it is possible that competitors may produce, develop, and commercialize therapeutics, or utilize other approaches such as gene therapy, to treat XLH. Most pediatric patients with XLH are managed using oral phosphate replacement and vitamin D therapy, which is relatively inexpensive and therefore may adversely affect our ability to commercialize KRN23, if approved, in some countries.

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With respect to rhGUS and rhPPCA, we are not aware of any other compounds currently in clinical development for MPS 7 or galactosialidosis, but it is possible that other companies may produce, develop, and commercialize compounds that might treat these diseases. Additionally, gene therapy and other therapeutic approaches may emerge for the treatment of lysosomal diseases. Bone marrow or stem cell transplants have also been used in MPS 7 and in other lysosomal storage diseases and represent a potential competing therapy. Stem cell transplants have been effective in treating soft tissue storage and in having an impact on brain disease, but have not to date proven effective in treating bone and connective tissue disease. Enzyme replacement therapy can have an impact on bone and connective tissue disease if patients are treated early.

With respect to triheptanoin, there are currently no approved drugs or treatments for patients with LC-FAOD or Glut1 DS. LC-FAOD is commonly treated with diet therapy and medium chain triglycerides, and triheptanoin would compete with MCT. Glut1 DS is commonly treated with ketogenic diet and anti-epileptic drugs. Triheptanoin may compete with these approaches, though it may also be used in combination. Although we believe that triheptanoin should be considered a drug and will be regulated that way, it is possible that other companies or individuals may attempt to produce triheptanoin for use by LC-FAOD, Glut1 DS, and other patients by attempting to sell the product via a nutraceutical or food pathway. It is also possible that other companies may produce, develop, and commercialize other medium-chain odd-chain fatty acids, or completely different compounds, to treat LC-FAOD and Glut1 DS. For example, B. Braun Medical Inc., or B. Braun, has applied for and received orphan drug designation for triheptanoin in Europe; we are not, however, aware of any ongoing development activities by B. Braun. Other companies may also utilize other approaches, such as gene therapy, to treat LC-FAOD and Glut1 DS.

With respect to SA-ER, although there are currently no approved drug therapies for the treatment of HIBM, it is possible that others may develop alternative approaches to the treatment of HIBM, including other metabolites from the sialic acid pathway, prodrugs, other drug therapies, and gene therapy. We are aware of a program at the National Institutes of Health that is investigating the use of another metabolite in the sialic acid pathway, N-acetyl mannosamine, or ManNAc, for the treatment of HIBM. This program is licensed to New Zealand Pharma, which manufactures ManNAc. The program recently completed a Phase 1 clinical study, and we anticipate that it will advance into Phase 2 testing.

Many of our competitors have substantially greater financial, technical, and human resources than we have. Additional mergers and acquisitions in the pharmaceutical industry may result in even more resources being concentrated in our competitors. Competition may increase further as a result of advances made in the commercial applicability of technologies and greater availability of capital for investment in these fields. Our success will be based in part on our ability to build and actively manage a portfolio of drugs that addresses unmet medical needs and creates value in patient therapy.

License Agreements

Kyowa Hakko Kirin

In August 2013, we entered into a collaboration and license agreement with Kyowa Hakko Kirin Co., Ltd., or KHK, pursuant to which we 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 we 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. Under the agreement, we also have a right of first negotiation with KHK to receive a license to develop and commercialize products in any non-diagnostic field, or in the field of orphan drugs outside of the profit share territory, the European territory, and Latin America.

In the field of orphan diseases, and except for ongoing studies being conducted by KHK, we will be the lead party for development activities in the profit share territory and in the European territory until, with respect to the profit share territory, the fifth anniversary of the first commercial sale in the United States in the first indication and, with respect to the European territory, the date on which marketing approval for a licensed product for the first indication is obtained in the European territory on a country-by-country basis; each such date is referred to herein as the applicable transition date. We will share the costs for development activities in the profit share

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territory and European territory conducted pursuant to the development plan before the applicable transition date equally with KHK. On the applicable transition date in the relevant territory, KHK will become the lead party and be responsible for these costs. However, we will continue to share the costs of the studies commenced prior to the applicable transition date equally with KHK. While we are the lead development party in the profit share territory, we must use commercially reasonable efforts to conduct development activities in at least one orphan disease indication other than XLH, as mutually agreed upon by KHK and us.

In the profit share territory, KHK will book sales of products and we will have the sole right to promote the products for a specified period of time, with KHK increasingly participating in the promotion of the products until five years from commercial launch, after which KHK will have the sole right to promote the products, subject to a limited promotion right retained by us. In the European territory, KHK will book sales of products and have the sole right to promote and sell the products. In Latin America, we will book sales of products and have the sole right to promote and sell the products.

The profit or loss from commercializing products in the profit share territory until the applicable transition date will be shared between us and KHK on a 50/50 basis. Thereafter, we will be entitled to receive a tiered double-digit revenue share in the mid to high twenty percent range in the profit share territory, intended to approximate the profit share. We will also be entitled to receive a royalty of up to 10% on net sales in the European territory. In Latin America, we will pay to KHK a low single-digit royalty on net sales. Our and KHK s obligations to pay royalties will continue on a country-by-country basis for so long as we or KHK, as applicable, are selling products in such country.

KHK will supply all quantities of product for clinical studies. KHK will also supply all quantities of product for commercial sales in the profit share territory and in Latin America. The supply price to us for commercial sales in the profit share territory and in Latin America will be determined based on a fixed percentage of net sales.

The collaboration and license agreement will continue for as long as products in the field of orphan diseases are sold in the profit share territory, European territory, or Latin America, unless the agreement is terminated in accordance with its terms.

KHK may terminate the entire agreement if we do not timely initiate a first pediatric study in XLH. In addition, KHK may terminate the agreement in certain countries or territories based upon our failure to meet certain milestones. Specifically, if we do not obtain U.S. or European marketing approval of KRN23 for the treatment of XLH by a certain date, or make a first commercial sale, on a country-by-country basis, in Latin America by certain deadlines, KHK may terminate the agreement only with respect to the applicable territory or country in which the milestone was not timely met. In certain circumstances, we have the right to obtain an extension of the applicable deadline by making a payment to KHK in the low single-digit to low double-digit millions of dollars, depending on the milestone. Also, in the event of the occurrence of certain excusable delays, the deadline for meeting the applicable milestone above is extended to account for the period of the delay. Furthermore, either party may terminate the agreement for the material breach or bankruptcy of the other party. In any event of termination by KHK, unless such termination is the result of KHK s termination for certain types of breach of the agreement by us, we may receive low single-digit to low double-digit royalties on net post-termination sales by KHK in one or more countries or territories, the amount of which varies depending on the timing of, and reason for, such termination. In any event of termination, our rights to KRN23 under the agreement and our obligations to share development costs will cease, and the program will revert to KHK, worldwide if the agreement is terminated as a whole or solely in the terminated countries if the agreement is terminated solely with respect to certain countries.

Saint Louis University

In November 2010, we entered into a license agreement with Saint Louis University, or SLU, wherein SLU granted us certain exclusive rights to intellectual property related to GUS. Under the terms of the license agreement, SLU granted us an exclusive worldwide license to make, have made, use, import, offer for sale, and sell therapeutics related to SLU s beta-glucuronidase product, such as our rhGUS product candidate, for use in the treatment of human diseases. Under this agreement, we agreed to use best efforts to develop and commercialize a licensed product as soon as practicable consistent with sound and reasonable business practices and judgment.

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Under the license agreement, we paid SLU an up-front fee of $10,000, which was recorded as a research and development expense. We will make a milestone payment of $100,000 upon approval of a glucuronidase-based enzyme therapy for treatment of MPS 7. Additionally, upon reaching a certain level of cumulative worldwide sales of the product, we will pay to SLU a low single-digit royalty on net sales of the licensed products in any country or region, subject to certain potential deductions. Our obligation to pay royalties to SLU continues on a country-by-country basis until the expiration of the last-to-expire licensed patent covering the product in such country or, in the United States, Japan, and the European Union, until the later expiration of any orphan drug exclusivity. We may deduct a portion of the royalty owed if a third-party license is required. We may terminate the agreement for convenience at any time and SLU may terminate the agreement for our material breach, bankruptcy, or challenge of the licensed patents or technology, and SLU may terminate the agreement or render our license non-exclusive if we fail to meet our diligence obligations. Unless terminated as set forth above, this license agreement continues in full force and effect until the latest of expiration of the last patent based on technology licensed under the agreement, at which point our license becomes fully paid.

St. Jude Children s Research Hospital

In September 2012, we entered into a license agreement with St. Jude Children s Research Hospital, or St. Jude, wherein St. Jude granted us certain exclusive rights to intellectual property related to rhPPCA. Under the terms of the license agreement, St. Jude granted us an exclusive license under certain know-how to research, develop, make, use, offer to sell, import, and otherwise commercialize and exploit certain PPCA protein products to treat, prevent, and/or diagnose galactosialidosis and other monogenetic diseases. We agreed to make commercially reasonable efforts to develop and commercialize at least one licensed product.

Under the license agreement, we paid St. Jude an up-front fee of $10,000, which was recorded as research and development expense. Additionally, we will pay to St. Jude a royalty of less than 1% on net sales of these products for so long as such products retain orphan drug exclusivity, on a country-by-country basis. We also received a right of first negotiation to receive an exclusive license under patents and know-how related to other uses of these products. We may terminate the agreement for convenience at any time and St. Jude may terminate the agreement for our material breach of the agreement. Unless terminated for convenience or material breach, as applicable, this license agreement continues in full force and effect, until our royalty obligations expire, at which point our license becomes irrevocable, perpetual, fully paid, and royalty-free.

Baylor Research Institute

In September 2012, we entered into a license agreement with Baylor Research Institute, or BRI, whereby we exclusively licensed certain intellectual property related to triheptanoin for North America and paid BRI an up-front fee of $250,000. The license includes patents, patent applications, know-how, and intellectual property related to the composition and formulation of triheptanoin as well as its use in treating a number of orphan diseases, including FAOD. The license grant includes the sole right to develop, manufacture, and commercialize licensed products for all human and animal uses. In June 2013, we exercised our option to license this intellectual property outside of North America and paid BRI the $750,000 fee associated with this option exercise. Under the license agreement, we are obligated to use commercially reasonable efforts to develop and commercialize licensed products in select orphan indications. If we fail to meet our diligence obligations with respect to a specified orphan indication or set of orphan indications, BRI may convert our license to a non-exclusive license with respect to such orphan indication or set of orphan indications until we receive regulatory approval for licensed products in the applicable orphan indication or set of orphan indications. We are also obligated to pay a mid-single digit royalty on net sales to BRI, subject to certain reductions and offsets. Our obligation to pay royalties to BRI continues on a licensed product-by-licensed product and country-by-country basis until the later of the expiration of the first regulatory exclusivity granted with respect to such product in such country or the expiration of the last-to-expire licensed patent claiming such product in such country, in each case in connection with approval in such country for FAOD or an orphan disease covered by our license from BRI. We may make future payments of up to $10.5 million contingent upon attainment of certain development milestones and $7.5 million if certain sales milestones are achieved. We may terminate the agreement for convenience at any

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time and either we or BRI may terminate the agreement for the material breach or bankruptcy of the other party. If we terminate for BRI s breach or bankruptcy, our license from BRI will remain in effect, subject to our continued payment of reduced milestones and royalties. Unless terminated for convenience or material breach or bankruptcy, as applicable, this license agreement continues in full force and effect, on a product-by-product and country-by-country basis, until our royalty obligations expire, at which point our license from BRI with respect to such product in such country becomes irrevocable, perpetual, fully paid and royalty-free.

Nobelpharma

In September 2010, we entered into a collaboration and license agreement with Nobelpharma Co., Ltd., or Nobelpharma. Under the terms of the 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 our licensed territory includes the rest of the world. The parties conduct development independently, and each party is obligated to make commercially reasonable efforts to file an investigational new drug application for licensed products in its territory and, in our case, to obtain patent term extensions and data exclusivity in Europe and North America, and share with the other party all data, documentation, and information that is generated in conducting such activities. Nobelpharma must use commercially reasonable efforts to supply us with the sialic acid drug substance. Either Nobelpharma or we can terminate this supply arrangement for convenience, at which point Nobelpharma would provide technical assistance to allow us to manufacture the sialic acid drug substance ourselves. If we choose to manufacture the sialic acid drug substance, Nobelpharma will have the right to purchase the sialic acid drug substance from us and we will use commercially reasonable efforts to supply Nobelpharma with the sialic acid drug substance.

Under the collaboration and license agreement, we have paid Nobelpharma approximately $110,000 as an upfront fee and approximately $495,000 in development milestone payments and also issued 76,567 shares of common stock to Nobelpharma. We are required to pay Nobelpharma a high single digit royalty on net sales of products in our territory and Nobelpharma is required to pay us a mid-single digit royalty on net sales in their territory (with the exception of Japan). Each party s obligation to pay royalties is subject to certain offsets and deductions, and is payable on a product-by-product and country-by-country basis until the expiration of the collaboration and license agreement. In addition, as of September 30, 2013, we are obligated to make a future payment to Nobelpharma of ¥200 million (approximately $2.0 million U.S. dollars) based upon achievement of a certain approval milestone. Either party may terminate the agreement for the material breach or bankruptcy of the other party. If either party terminates the agreement, the terminating party s license will become irrevocable and royalty-free. Unless terminated for material breach or bankruptcy, as applicable, this license agreement continues in full force and effect, on a country-by-country basis, until the date of the first launch of a generic product of the licensed product in a country.

AAI Pharma

In March 2011, we entered into a license agreement with AAIPharma Services Corp., or AAI Pharma. Under the terms of this license agreement, AAI Pharma granted us a fully paid-up, royalty-free, exclusive, perpetual, and irrevocable license to research, develop, make, have made, use, import, offer for sale, and sell products incorporating AAI Pharma s controlled release matrix solid dose oral tablet technology for use in connection with sialic acid for the treatment of HIBM or distal myopathy with rimmed vacuoles. Under the license agreement, we will pay a mid-single digit percentage of any sublicense revenue received by us related to the sublicense of AAI Pharma technology. As consideration, we agreed to provide preclinical and clinical data to AAI Pharma. AAI Pharma is responsible for patent prosecution and maintenance, subject to our right to review and comment on such prosecution and maintenance. We may terminate the agreement for convenience at any time and either party may terminate the agreement for the material breach or bankruptcy of the other party.

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HIBM Research Group

In April 2012, we entered into an exclusive license agreement with HIBM Research Group, or HRG, wherein HRG granted us an exclusive, worldwide license to certain intellectual property related to the treatment of HIBM and related conditions using substrate replacement therapy.

Under the terms of license agreement, we paid HRG an up-front fee of $25,000, which was recorded as a research and development expense. We will make future payments contingent upon attainment of various development and approval milestones of up to $300,000 in the aggregate. Additionally, we will pay to HRG a royalty of less than 1% of net sales of products, if any. Our obligation to pay royalties to HRG continues on a product-by-product and country-by-country basis until the expiration of the last-to-expire licensed patent claiming such product in such country, or the later expiration of orphan drug exclusivity in certain countries. We are obligated to make commercially reasonable efforts to develop and commercialize a substrate replacement therapy for HIBM. We may terminate the agreement for convenience at any time and either party may terminate the agreement for the material breach or bankruptcy of the other party. We must also terminate the agreement if we terminate our HIBM substrate replacement therapy program. Unless terminated for convenience, for our termination of our HIBM substrate replacement therapy program, or for material breach or bankruptcy, as applicable, this license agreement continues in full force and effect, on a product-by-product and country-by-country basis, until the expiration date of the last-to-expire licensed patent claiming such product in such country, or the later expiration of orphan drug exclusivity in certain countries, at which point our license becomes irrevocable, perpetual, fully paid, and royalty-free.

Patents and Proprietary Rights

The proprietary nature of, and protection for, our product candidates, processes, and know-how are important to our business. Our success depends in part on our ability to protect the proprietary nature of our product candidates, technology, and know-how, to operate without infringing on the proprietary rights of others, and to prevent others from infringing our proprietary rights. We seek patent protection in the United States and internationally for our product candidates and other technology. Our policy is to patent or in-license the technology, inventions and improvements that we consider important to the development of our business. In addition to patent protection, we intend to use other means to protect our proprietary rights, including pursuing marketing or data exclusivity periods, orphan drug status, and similar rights that are available under regulatory provisions in certain countries, including the United States, Europe, Japan, and China. See U.S. Government Regulation Orphan Designation and Exclusivity, U.S. Government Regulation Pediatric Studies and Exclusivity, U.S. Government Regulation Patent Term Restoration, U.S. Government Regulation Biosimilars and Exclusivity, U.S. Government Regulation Abbreviated New Drug Applications for Generic Drugs, U.S. Government Regulation Hatch-Waxman Patent Certification and the 30-Month Stay, and European Union/Rest of World Government Regulation Orphan Designation and Exclusivity below for additional information.

We also rely on trade secrets, know-how, and continuing innovation to develop and maintain our competitive position. We cannot be certain that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents granted to us in the future will be commercially useful in protecting our technology.

We seek regulatory approval for our products in disease areas with high unmet medical need, great market potential, and where we have a proprietary position through patents covering various aspects of our products, such as composition, dosage, formulation, use, and manufacturing process, among others. Our success depends on an intellectual property portfolio that supports our future revenue streams and erects barriers to our competitors. We are maintaining and building our patent portfolio through filing new patent applications, prosecuting existing applications, and licensing and acquiring new patents and patent applications.

Despite these measures, any of our intellectual property and proprietary rights could be challenged, invalidated, circumvented, infringed or misappropriated, or such intellectual property and proprietary rights may not be sufficient to permit us to take advantage of current market trends or otherwise to provide competitive advantages. For more information, please see Risks Related to our Intellectual Property.

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As of January 10, 2014, we own 11 pending U.S. patent applications and corresponding patents and patent applications internationally. In addition, as of January 10, 2014, we have licensed 10 issued U.S. patents and 13 pending U.S. patent applications as well as corresponding foreign patents and applications from third parties, on an exclusive basis. With respect to our issued patents in the United States and Europe, we are also entitled to obtain a patent term extension to extend the patent expiration date. For example, in the United States, we can apply for a patent term extension of up to five years for one of the patents covering a product once the product is approved by the FDA. The exact duration of the extension depends on the time we spend in clinical studies as well as getting a new drug application approval from the FDA. The patent portfolios for our five leading product candidates as of January 10, 2014 are summarized below.

KRN23

We have rights from KHK to patents and patent applications relating to KRN23, a fully human monoclonal antibody against FGF23, and its use for the treatment of XLH and various other hypophosphatemic conditions. Pursuant to this license, we share rights to 20 issued patents, including 3 U.S. patents and 1 pending U.S. application and patents and applications in other jurisdictions covering generic and specific antibodies against FGF23 as well as their use for the treatment of XLH and related conditions. The patent terms for issued patents in the United States are from 2022 to 2029 (without patent term extension). The projected patent term for pending applications in the United States is 2028. We intend to pursue marketing and orphan drug exclusivity periods that are available to us under regulatory provisions in certain countries. KRN23 has received orphan drug designation in the United States.

rhGUS

We have no issued patents covering rhGUS but we are in the process of filing patent applications directed to compositions with certain characteristics that are useful for the enzyme replacement therapy for the treatment of multi-system lysosomal storage disease. Throughout clinical research and development, we also intend to file patent applications directed to various aspects of the treatment therapy including dosage, regiment, formulation, manufacturing, etc. We intend to pursue marketing and orphan drug exclusivity periods that are available under regulatory provisions in certain countries. rhGUS has received orphan drug designation in both the United States and Europe.

rhPPCA

We have no issued patents or patent applications filed for rhPPCA, although it is partially protected by proprietary know-how licensed from St. Jude Children s Hospital. We intend to build a patent portfolio directed to compositions with certain characteristics that are useful for the enzyme replacement therapy for the treatment of autosomal recessive lysosomal storage disease as well as various aspects of the treatment therapy including dosage, regimen, formulation, manufacturing, etc. We intend to pursue marketing and orphan drug exclusivity periods that are available under regulatory provisions in certain countries.

Triheptanoin

We are the licensee or owner of patents and patent applications relating to triheptanoin and its use for a number of diseases including FAOD and Glut1 DS. In particular, we have an exclusive license from Baylor Research Institute, or BRI, with respect to its triheptanoin patent portfolio. We have licensed from BRI 24 issued patents, including 7 U.S. patents and 8 pending U.S. applications and patents and applications in other jurisdictions covering composition, formulation, use and manufacturing of triheptanoin and related odd carbon fatty acids. The patent terms for issued patents in the United States are from 2020 to 2024 (without patent term extension). The projected patent terms for pending applications in the United States are from 2020 to 2034. We intend to pursue marketing and orphan drug exclusivity periods that are available under regulatory provisions in certain countries.

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SA-ER

We are the licensee or owner of patents and patent applications relating to sialic acid and its use for the treatment of HIBM. We have 10 pending U.S. applications and patents and applications in other jurisdictions covering the use of sialic acid for the treatment of HIBM, biomarkers useful for such treatment as well as extended release formulations of sialic acid. The projected patent terms for pending applications in the United States are from 2028 to 2034.

We intend to pursue marketing and orphan drug exclusivity periods that are available under regulatory provisions in certain countries. SA-ER has received orphan drug designation in both the United States and the European Union.

Trademarks

We have filed U.S. trademark applications for ULTRAGENYX and ULTRAGENYX PHARMACEUTICAL.

Other

We rely upon unpatented trade secrets, know-how, and continuing technological innovation to develop and maintain our competitive position. We seek to protect our ownership of know-how and trade secrets through an active program of legal mechanisms including assignments, confidentiality agreements, material transfer agreements, research collaborations, and licenses.

Manufacturing

We currently contract with third parties for the manufacturing and testing of our product candidates for preclinical studies and clinical studies and intend to do so in the future. We do not own or operate manufacturing facilities for the production of clinical quantities of our product candidates. We currently have no plans to build our own clinical or commercial scale manufacturing capabilities. The use of contracted manufacturing and reliance on collaboration partners is relatively cost-efficient and has eliminated the need for our direct investment in manufacturing facilities and additional staff early in development. Although we rely on contract manufacturers, we have personnel with extensive manufacturing experience to oversee our contract manufacturers.

To date, our third-party manufacturers have met our manufacturing requirements. We expect third-party manufacturers to be capable of providing sufficient quantities of our product candidates to meet anticipated full scale commercial demands. To meet our projected needs for commercial manufacturing, third parties with whom we currently work might need to increase their scale of production or we will need to secure alternate suppliers. We believe that there are alternate sources of supply that can satisfy our clinical and commercial requirements, although we cannot be certain that identifying and establishing relationships with such sources, if necessary, would not result in significant delay or material additional costs.

KRN23

The drug substance and drug product for KRN23 are made by KHK in Japan under the collaboration and license agreement with KHK. The cell line to produce KRN23 is specific for this product and is in KHK s control. All other raw materials are commercially available.

rhGUS

rhGUS drug substance and drug product are manufactured by Rentschler Biotechnologie GmbH, or Rentschler, under a development and clinical supply agreement executed in August 2012. Pursuant to the supply agreement, we have agreed not to source larger quantities of drug substance or drug product from another supplier than from Rentschler in any given year. The supply agreement will continue in full force and effect until all services have been completed or terminated per the terms of the supply agreement. Either party may terminate the supply agreement if the other party fails to pay any sum payable under the supply agreement within 30 days

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after a written demand is issued after the original due date, if the other party makes a material misrepresentation or commits a material breach of its obligations under the supply agreement and fails to cure such breach within specified time periods if curable, if the other party ceases to carry on its business for a period no less than 60 days, or if a party experiences certain insolvency events. Additionally, either party may terminate the supply agreement upon 30 days prior written notice if the Steering Committee concludes that the services required under the supply agreement cannot be performed and we may terminate the agreement at any time before completion of the services rendered pursuant to the agreement upon 60 days prior written notice. The cell line to produce rhGUS is specific for this product and is in our control and stored in multiple secure locations. All other raw materials are commercially available.

rhPPCA

No supplier has yet been selected for rhPPCA. The cell line to produce rhPPCA is specific for this product and is in our control and stored in multiple secure locations. The process to produce rhPPCA will only contain commercially available materials.

Triheptanoin

The pharmaceutical-grade drug substance for triheptanoin is manufactured by Cremer Oleo GmbH & Co. KG in Germany under an exclusive worldwide supply agreement, subject to certain limitations, executed in 2012. The supply agreement has an initial term of three years; thereafter, the agreement shall be automatically renewed for additional two-year periods unless either party notifies the other party of its intention not to renew in writing at least three calendar months before the expiration of the then current term. Additionally, if a party materially breaches an obligation under the agreement and does not cure such breach within 60 days of receiving notice of the breach from the non-breaching party, the non-breaching party may terminate the agreement immediately upon written notice to the breaching party. Triheptanoin drug product manufacturing has been done with more than one party and is not considered a very specialized task.

SA-ER

The drug substance for SA-ER is currently manufactured by Sanyo Fine Co., Ltd. in Japan through the license agreement with Nobelpharma. The SA-ER drug product is manufactured by AAI Pharma under our license agreement and accompanying purchase orders with AAI Pharma. We are in the process of identifying secondary sources of drug substance and drug product for SA-ER. Manufacture of the drug substance requires a specialized enzyme-catalyzed step, and a secondary source of the enzyme itself is also under development. All raw materials to produce the drug substance and drug product are commercially available. The cell line to produce the specialized enyme is under our contol and is stored in multiple secured locations.

Sales and Marketing

We currently intend to build the commercial infrastructure in the United States and Europe necessary to effectively support the commercialization of all of our product candidates, if and when we believe a regulatory approval of the first of such product candidates in a particular geographic market appears imminent. The commercial infrastructure for orphan products typically consists of a targeted, specialty sales force that calls on a limited and focused group of physicians supported by sales management, medical liaisons, internal sales support, an internal marketing group, and distribution support. One challenge unique to commercializing therapies for rare diseases is the difficulty in identifying eligible patients due to the very small and sometimes heterogeneous disease populations. Our management team is experienced in maximizing patient identification for both clinical development and commercialization purposes in rare diseases.

Additional capabilities important to the orphan marketplace include the management of key accounts such as managed care organizations, group-purchasing organizations, specialty pharmacies, and government accounts. To develop the appropriate commercial infrastructure, we will have to invest significant amounts of financial and management resources, some of which will be committed prior to any confirmation that any of our product candidates will be approved.

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Outside of the United States and Europe, where appropriate, we may elect in the future to utilize strategic partners, distributors, or contract sales forces to assist in the commercialization of our products. In certain instances we may consider building our own commercial infrastructure.

Government Regulation

Government authorities in the United States (including federal, state, and local authorities) and in other countries, extensively regulate, among other things, the manufacturing, research and clinical development, marketing, labeling and packaging, storage, distribution, post-approval monitoring and reporting, advertising and promotion, pricing, and export and import of pharmaceutical products, such as those we are developing. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local, and foreign statutes and regulations require the expenditure of substantial time and financial resources.

U.S. Government Regulation

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations, and biologics under the FDCA and the Public Health Service Act, or PHSA, and its implementing regulations. FDA approval is required before any new unapproved drug or dosage form, including a new use of a previously approved drug, can be marketed in the United States. Drugs and biologics are also subject to other federal, state, and local statutes and regulations. If we fail to comply with applicable FDA or other requirements at any time during the drug development process, clinical testing, the approval process or after approval, we may become subject to administrative or judicial sanctions. These sanctions could include the FDA s refusal to approve pending applications, license suspension or revocation, withdrawal of an approval, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties or criminal prosecution. Any FDA enforcement action could have a material adverse effect on us.

The process required by the FDA before product candidates may be marketed in the United States generally involves the following:

- completion of extensive preclinical laboratory tests and preclinical animal studies, all performed in accordance with the Good Laboratory Practices, or GLP, regulations;
- submission to the FDA of an investigational new drug application, or IND, which must become effective before human clinical studies may begin and must be updated annually;
- approval by an independent institutional review board, or IRB, or ethics committee representing each clinical site before each clinical study may be initiated;
- performance of adequate and well-controlled human clinical studies to establish the safety and efficacy of the product candidate for each proposed indication;
- preparation of and submission to the FDA of a new drug application, or NDA, or biologics license application, or BLA, after completion of all pivotal clinical studies;
- potential review of the product application by an FDA advisory committee, where appropriate and if applicable;
- a determination by the FDA within 60 days of its receipt of an NDA or BLA to file the application for review;

satisfactory completion of an FDA pre-approval inspection of the manufacturing facilities where the proposed product drug substance is produced to assess compliance with current Good Manufacturing Practices, or cGMP; and

FDA review and approval of an NDA or BLA prior to any commercial marketing or sale of the drug in the United States.

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The preclinical and clinical testing and approval process requires substantial time, effort, and financial resources, and we cannot be certain that any approvals for our product candidates will be granted on a timely basis, if at all.

An IND is a request for authorization from the FDA to administer an investigational new drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocol(s) for human studies. The IND also includes results of animal and *in vitro* studies assessing the toxicology, pharmacokinetics, pharmacology, and pharmacodynamic characteristics of the product; chemistry, manufacturing, and controls information; and any available human data or literature to support the use of the investigational new drug. An IND must become effective before human clinical trials may begin. An IND will automatically become effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to the proposed clinical studies. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before clinical studies can begin. Accordingly, submission of an IND may or may not result in the FDA allowing clinical studies to commence.

Clinical Studies

Clinical studies involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with current Good Clinical Practices, or cGCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical study. Clinical studies are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety, and the efficacy criteria to be evaluated. A protocol for each clinical study and any subsequent protocol amendments must be submitted to the FDA as part of the IND. Additionally, approval must also be obtained from each clinical study site s institutional review board, or IRB, before the studies may be initiated, and the IRB must monitor the study until completed. There are also requirements governing the reporting of ongoing clinical studies and clinical study results to public registries.

The clinical investigation of a drug is generally divided into three or four phases. Although the phases are usually conducted sequentially, they may overlap or be combined.

Phase 1. The drug is initially introduced into healthy human subjects or patients with the target disease or condition. These studies are designed to evaluate the safety, dosage tolerance, metabolism and pharmacologic actions of the investigational new drug in humans, the side effects associated with increasing doses, and if possible, to gain early evidence on effectiveness.

Phase 2. The drug is administered to a limited patient population to evaluate dosage tolerance and optimal dosage, identify possible adverse side effects and safety risks, and preliminarily evaluate efficacy.

Phase 3. The drug is administered to an expanded patient population, generally at geographically dispersed clinical study sites to generate enough data to statistically evaluate dosage, clinical effectiveness and safety, to establish the overall benefit-risk relationship of the investigational new drug product, and to provide an adequate basis for product approval.

Phase 4. In some cases, the FDA may condition approval of an NDA or BLA for a product candidate on the sponsor s agreement to conduct additional clinical studies after approval. In other cases, a sponsor may voluntarily conduct additional clinical studies after approval to gain more information about the drug. Such post-approval studies are typically referred to as Phase 4 clinical studies.

A pivotal study is a clinical study that adequately meets regulatory agency requirements for the evaluation of a drug candidate s efficacy and safety such that it can be used to justify the approval of the product. Generally, pivotal studies are Phase 3 studies, but the FDA may accept results from Phase 2 studies if the study design provides a well-controlled and reliable assessment of clinical benefit, particularly in situations where there is an unmet medical need and the results are sufficiently robust.

The FDA, the IRB, or the clinical study sponsor may suspend or terminate a clinical study at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk.

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Additionally, some clinical studies are overseen by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study. We may also suspend or terminate a clinical study based on evolving business objectives and/or competitive climate.

The clinical study process can take three to ten years or more to complete, and there can be no assurance that the data collected will support FDA approval or licensure of the product.

Submission of an NDA or BLA to the FDA

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, detailed investigational new drug product information is submitted to the FDA in the form of an NDA or BLA requesting approval to market the product for one or more indications. Under federal law, the submission of most NDAs and BLAs is subject to an application user fee. For fiscal year 2014, the application user fee exceeds $2.1 million, and the sponsor of an approved NDA or BLA is also subject to annual product and establishment user fees, set at $104,060 per product and $554,600 per establishment. These fees are typically increased annually. Applications for orphan drug products are exempted from the NDA and BLA user fees and may be exempted from product and establishment user fees, unless the application includes an indication for other than a rare disease or condition.

An NDA or BLA must include all relevant data available from pertinent preclinical and clinical studies, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product s chemistry, manufacturing, controls, and proposed labeling, among other things. Data can come from company-sponsored clinical studies intended to test the safety and effectiveness of a use of a product, or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and effectiveness of the investigational new drug product to the satisfaction of the FDA.

Once an NDA or BLA has been submitted, the FDA s goal is to review the application within ten months after it accepts the application for filing, or, if the application relates to an unmet medical need in a serious or life-threatening indication, six months after the FDA accepts the application for filing. The review process is often significantly extended by FDA requests for additional information or clarification.

Before approving an NDA or BLA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA or BLA, the FDA will typically inspect one or more clinical sites to assure compliance with cGCP.

The FDA is required to refer an application for a novel drug to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

The FDA s Decision on an NDA or BLA

After the FDA evaluates the NDA or BLA and conducts inspections of manufacturing facilities where the drug product and/or its drug substance will be produced, it may issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the application is not ready for approval. A Complete Response Letter may require additional clinical data and/or an additional pivotal Phase 3 clinical study(ies), and/or other significant, expensive and time-consuming requirements related to clinical studies, preclinical studies or manufacturing. Even if such additional information

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is submitted, the FDA may ultimately decide that the NDA or BLA does not satisfy the criteria for approval. The FDA could also approve the NDA or BLA with a Risk Evaluation and Mitigation Strategy, or REMS, plan to mitigate risks, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling, development of adequate controls and specifications, or a commitment to conduct one or more post-market studies or clinical studies. Such post-market testing may include Phase 4 clinical studies and surveillance to further assess and monitor the product s safety and effectiveness after commercialization. Also, new government requirements, including those resulting from new legislation, may be established, or the FDA s policies may change, which could delay or prevent regulatory approval of our products under development.

Expedited Review and Accelerated Approval Programs

A sponsor may seek approval of its product candidate under programs designed to accelerate FDA s review and approval of NDAs and BLAs. For example, Fast Track Designation may be granted to a drug intended for treatment of a serious or life-threatening disease or condition that has potential to address unmet medical needs for the disease or condition. The key benefits of fast track designation are the eligibility for priority review, rolling review (submission of portions of an application before the complete marketing application is submitted), and accelerated approval, if relevant criteria are met. Based on results of the Phase 3 clinical study(ies) submitted in an NDA or BLA, upon the request of an applicant, the FDA may grant the NDA or BLA a priority review designation, which sets the target date for FDA action on the application at six months after the FDA accepts the application for filing. Priority review is granted where there is evidence that the proposed product would be a significant improvement in the safety or effectiveness of the treatment, diagnosis, or prevention of a serious condition. If criteria are not met for priority review, the application is subject to the standard FDA review period of ten months after FDA accepts the application for filing. Priority review designation does not change the scientific/medical standard for approval or the quality of evidence necessary to support approval.

Under the accelerated approval program, the FDA may approve an NDA or BLA on the basis of either a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Post-marketing studies or completion of ongoing studies after marketing approval are generally required to verify the drug s clinical benefit in relationship to the surrogate endpoint or ultimate outcome in relationship to the clinical benefit. In addition, the Food and Drug Administration Safety and Innovation Act, or FDASIA, which was enacted and signed into law in 2012, established the new Breakthrough Therapy designation. A sponsor may seek FDA designation of its product candidate as a breakthrough therapy if the drug is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

Drug manufacturers are subject to periodic unannounced inspections by the FDA and state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated, and,

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depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

We rely, and expect to continue to rely, on third parties for the production of clinical quantities of our product candidates, and expect to rely in the future on third parties for the production of commercial quantities. Future FDA and state inspections may identify compliance issues at our facilities or at the facilities of our contract manufacturers that may disrupt production or distribution, or require substantial resources to correct. In addition, discovery of previously unknown problems with a product or the failure to comply with applicable requirements may result in restrictions on a product, manufacturer or holder of an approved NDA or BLA, including withdrawal or recall of the product from the market or other voluntary, FDA-initiated or judicial action that could delay or prohibit further marketing. Also, new government requirements, including those resulting from new legislation, may be established, or the FDA s policies may change, which could delay or prevent regulatory approval of our products under development.

The FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical studies;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising, and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

Orphan Designation and Exclusivity

The FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the United States, or if it affects more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and making the drug for this type of disease or condition will be recovered from sales in the United States.

Orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical study costs, tax advantages, and user-fee waivers. In addition, if a product receives FDA approval for the indication for which it has orphan designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity.

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Pediatric Studies and Exclusivity

NDAs and BLAs must contain data (or a proposal for post-marketing activity) to assess the safety and effectiveness of an investigational new drug product for the claimed indications in all relevant pediatric populations in order to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults or full or partial waivers if certain criteria are met. Discussions about pediatric development plans can be discussed with the FDA at any time, but usually occur any time between the end-of-Phase II meeting and submission of the NDA or BLA. The requirements for pediatric data do not apply to any drug for an indication for which orphan designation has been granted.

Pediatric exclusivity is another type of non-patent exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the five-year and three-year non-patent and orphan exclusivity. This six-month exclusivity may be granted if an NDA or BLA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical study is deemed to fairly respond to the FDA s request, the additional protection is granted. If reports of FDA-requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot accept or approve another application relying on the NDA or BLA sponsor s data.

Patent Term Restoration

Depending upon the timing, duration, and specifics of the FDA approval of the use of our product candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product s approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA or BLA, plus the time between the submission date and the approval of that application. Only one patent applicable to an approved product is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The U.S. Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we may apply for restoration of patent term for one of our currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical studies and other factors involved in the filing of the relevant NDA or BLA.

Biosimilars and Exclusivity

The Patient Protection and Affordable Care Act, or Affordable Care Act, signed into law on March 23, 2010, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCI Act, which created an abbreviated approval pathway for biological products shown to be similar to, or interchangeable with, an FDA-licensed reference biological product. This amendment to the PHSA attempts to minimize duplicative testing. Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical study or studies. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product and, for products administered multiple times, the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. However, complexities associated with the

larger, and often more complex, structure of biological products, as well as the process by which such products are manufactured, pose significant hurdles to implementation that are still being worked out by the FDA.

A reference biologic is granted twelve years of exclusivity from the time of first licensure of the reference product. The first biologic product submitted under the abbreviated approval pathway that is determined to be interchangeable with the reference product has exclusivity against other biologics submitting under the abbreviated approval pathway for the lesser of (i) one year after the first commercial marketing, (ii) eighteen months after approval if there is no legal challenge, (iii) eighteen months after the resolution in the applicant s favor of a lawsuit challenging the biologics patents if an application has been submitted, or (iv) 42 months after the application has been approved if a lawsuit is ongoing within the 42-month period.

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Hatch-Waxman Act, Congress authorized the FDA to approve generic drugs that are the same as drugs previously approved by the FDA under the NDA provisions of the statute. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the agency. In support of such applications, a generic manufacturer may rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference listed drug, or RLD.

Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, and the strength of the drug. At the same time, the FDA must also determine that the generic drug is bioequivalent to the innovator drug. Under the statute, a generic drug is bioequivalent to an RLD if the rate and extent of absorption of the [generic] drug do not show a significant difference from the rate and extent of absorption of the listed drug. . . .

Upon approval of an ANDA, the FDA indicates that the generic product is therapeutically equivalent to the RLD and it assigns a therapeutic equivalence rating to the approved generic drug in its publication Approved Drug Products with Therapeutic Equivalence Evaluations, also referred to as the Orange Book. Physicians and pharmacists consider an AB therapeutic equivalence rating to mean that a generic drug is fully substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, the FDA s designation of an AB rating often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or patient.

The FDCA provides a period of five years of non-patent exclusivity for a new drug containing a new chemical entity. In cases where such exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the applicant may submit its application four years following the original product approval. The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication.

Hatch-Waxman Patent Certification and the 30-Month Stay

Upon approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant s product or a method of using the product. Each of the patents listed by the NDA sponsor is published in the Orange Book. When an ANDA applicant files its application with the FDA, the applicant is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval.

Specifically, the applicant must certify with respect to each patent that:

- the required patent information has not been filed;
- the listed patent has expired;
- the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or

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the listed patent is invalid, unenforceable or will not be infringed by the new product.

A certification that the new product will not infringe the already approved product s listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not challenge the listed patents or indicates that it is not seeking approval of a patented method of use, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired.

If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months after the receipt of the Paragraph IV notice, expiration of the patent, or a decision in the infringement case that is favorable to the ANDA applicant.

European Union/Rest of World Government Regulation

In addition to regulations in the United States, we will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical studies and any commercial sales and distribution of our products.

Whether or not we obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical studies or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical study application much like the IND prior to the commencement of human clinical studies. In the European Union, for example, a clinical study application, or CTA, must be submitted for each clinical protocol to each country s national health authority and an independent ethics committee, much like the FDA and IRB, respectively. Once the CTA is accepted in accordance with a country s requirements, the clinical study may proceed.

The requirements and process governing the conduct of clinical studies vary from country to country. In all cases, the clinical studies are conducted in accordance with cGCP, the applicable regulatory requirements, and the ethical principles that have their origin in the Declaration of Helsinki.

To obtain regulatory approval of an investigational medicinal product under European Union regulatory systems, we must submit a marketing authorization application. The content of the NDA or BLA filed in the United States is similar to that required in the European Union, with the exception of, among other things, country-specific document requirements.

For other countries outside of the European Union, such as countries in Eastern Europe, Latin America or Asia, the requirements governing product licensing, pricing, and reimbursement vary from country to country.

Countries that are part of the European Union, as well as countries outside of the European Union, have their own governing bodies, requirements, and processes with respect to the approval of pharmaceutical products. If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Authorization Procedures in the European Union

Medicines can be authorized in the European Union by using either the centralized authorization procedure or national authorization procedures.

Centralized procedure. The EMA implemented the centralized procedure for the approval of human medicines to facilitate marketing authorizations that are valid throughout the European Economic Area, or EEA, which is comprised of the 28 member states of the European Union plus Norway, Iceland, and Lichtenstein. This procedure results in a single marketing authorization issued by the EMA that is valid

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across the EEA. The centralized procedure is compulsory for human medicines that are: derived from biotechnology processes, such as genetic engineering, contain a new active substance indicated for the treatment of certain diseases, such as HIV/AIDS, cancer, diabetes, neurodegenerative disorders or autoimmune diseases and other immune dysfunctions, and officially designated orphan medicines.

For medicines that do not fall within these categories, an applicant has the option of submitting an application for a centralized marketing authorization to the European Commission following a favorable opinion by the EMA, as long as the medicine concerned is a significant therapeutic, scientific or technical innovation, or if its authorization would be in the interest of public health.

National authorization procedures. There are also two other possible routes to authorize medicinal products in several European Union countries, which are available for investigational medicinal products that fall outside the scope of the centralized procedure:

Decentralized procedure. Using the decentralized procedure, an applicant may apply for simultaneous authorization in more than one European Union country of medicinal products that have not yet been authorized in any European Union country and that do not fall within the mandatory scope of the centralized procedure.

Mutual recognition procedure. In the mutual recognition procedure, a medicine is first authorized in one European Union Member State, in accordance with the national procedures of that country. Following this, further marketing authorizations can be sought from other European Union countries in a procedure whereby the countries concerned agree to recognize the validity of the original, national marketing authorization.

In some cases, a Pediatric Investigation Plan, and/or a request for waiver or deferral, is required for submission prior to submitting a marketing authorization application. A PIP describes, among other things, proposed pediatric studies and their timing relative to clinical studies in adults.

New Chemical Entity Exclusivity

In the European Union, new chemical entities, sometimes referred to as new active substances, qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. This data exclusivity, if granted, prevents regulatory authorities in the European Union from referencing the innovator s data to assess a generic (abbreviated) application for eight years, after which generic marketing authorization can be submitted, and the innovator s data may be referenced, but not approved for two years. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies.

Orphan Designation and Exclusivity

In the European Union, the EMA s Committee for Orphan Medicinal Products, or COMP, grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions affecting not more than 5 in 10,000 persons in the European Union Community and for which no satisfactory method of diagnosis, prevention, or treatment has been authorized (or the product would be a significant benefit to those affected). Additionally, designation is granted for products intended for the diagnosis, prevention, or treatment of a life-threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the necessary investment in developing the medicinal product.

In the European Union, orphan drug designation entitles a party to financial incentives such as reduction of fees or fee waivers and 10 years of market exclusivity is granted following medicinal product approval. This period may be reduced to six years if the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity.

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Orphan drug designation must be requested before submitting an application for marketing approval. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

Exceptional Circumstances/Conditional Approval

Orphan drugs or drugs with unmet medical needs may be eligible for EU approval under exceptional circumstances or with conditional approval. Approval under exceptional circumstances is applicable to orphan products and is used when an applicant is unable to provide comprehensive data on the efficacy and safety under normal conditions of use because the indication for which the product is intended is encountered so rarely that the applicant cannot reasonably be expected to provide comprehensive evidence, when the present state of scientific knowledge does not allow comprehensive information to be provided, or when it is medically unethical to collect such information. Conditional marketing authorization is applicable to orphan medicinal products, medicinal products for seriously debilitating or life-threatening diseases, or medicinal products to be used in emergency situations in response to recognized public threats. Conditional marketing authorization can be granted on the basis of less complete data than is normally required in order to meet unmet medical needs and in the interest of public health, provided the risk-benefit balance is positive, it is likely that the applicant will be able to provide the comprehensive clinical data, and unmet medical needs will be fulfilled. Conditional marketing authorization is subject to certain specific obligations to be reviewed annually.

Accelerated Review

Under the Centralized Procedure in the European Union, the maximum timeframe for the evaluation of a marketing authorization application is 210 days (excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the EMA s Committee for Medicinal Products for Human Use, or CHMP). Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, particularly from the point of view of therapeutic innovation. In this circumstance, EMA ensures that the opinion of the CHMP is given within 150 days, excluding clock stops.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any drug products for which we obtain regulatory approval. In the United States and markets in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend in part on the availability of coverage and reimbursement from third-party payors. Third-party payors include government authorities, managed care providers, private health insurers and other organizations. The process for determining whether a payor will provide coverage for a drug product may be separate from the process for setting the reimbursement rate that the payor will pay for the drug product. Third-party payors may limit coverage to specific drug products on an approved list, or formulary, which might not include all of the FDA-approved drugs for a particular indication. Moreover, a payor s decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

Third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. In order to obtain coverage and reimbursement for any product that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain regulatory approvals. Our product candidates may not be considered medically necessary or cost-effective. If third-party payors do not consider a product to be cost-effective compared to other available therapies, they may not cover the product after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow a company to sell its products at a profit.

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The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid health care costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. By way of example, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively, the Healthcare Reform Law, contains provisions that may reduce the profitability of drug products, including, for example, increased rebates for drugs sold to Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies share of sales to federal health care programs. Adoption of government controls and measures, and tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceuticals.

In the European Community, governments influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national health care systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed to by the government. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical studies that compare the cost-effectiveness of a particular product candidate to currently available therapies. Other member states allow companies to fix their own prices for medicines, but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country.

The marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, an increasing emphasis on cost containment measures in the United States and other countries has increased and we expect will continue to increase the pressure on pharmaceutical pricing. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Other Healthcare Laws and Compliance Requirements

If we obtain regulatory approval for any of our product candidates, we may be subject to various federal and state laws targeting fraud and abuse in the healthcare industry. These laws may impact, among other things, our proposed sales, marketing and education programs. In addition, we may be subject to patient privacy regulation by both the federal government and the states in which we conduct our business. The laws that may affect our ability to operate include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, the purchase or recommendation of an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;

- federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payers that are false or fraudulent;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;

- the federal transparency laws, including the federal Physician Payment Sunshine Act, that requires drug manufacturers to disclose payments and other transfers of value provided to physicians and teaching hospitals;

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HIPAA, as amended by the Health Information Technology and Clinical Health Act, or HITECH, and its implementing regulations, which imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information; and

state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payer, including commercial insurers, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

The Healthcare Reform Law broadened the reach of the fraud and abuse laws by, among other things, amending the intent requirement of the federal Anti-Kickback Statute and the applicable criminal healthcare fraud statutes contained within 42 U.S.C. § 1320a-7b, effective March 23, 2010. Pursuant to the statutory amendment, a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, the Healthcare Reform Law provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act (discussed below) or the civil monetary penalties statute. Many states have adopted laws similar to the federal Anti-Kickback Statute, some of which apply to the referral of patients for healthcare items or services reimbursed by any source, not only the Medicare and Medicaid programs.

We are also subject to the Foreign Corrupt Practices Act, or FCPA, which prohibits improper payments or offers of payments to foreign governments and their officials for the purpose of obtaining or retaining business. Safeguards we implement to discourage improper payments or offers of payments by our employees, consultants, and others may be ineffective, and violations of the FCPA and similar laws may result in severe criminal or civil sanctions, or other liabilities or proceedings against us, any of which would likely harm our reputation, business, financial condition and result of operations.

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

Employees

As of December 31, 2013, we had 59 full-time employees. None of our employees is represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Research and Development

We recognized $4.7 million and $12.6 million in research and development expense in the years ended December 31, 2011 and 2012, respectively, and $19.6 million in research and development expense for the nine months ended September 30, 2013.

Facilities

Our offices are located at two leased facilities: a 19,916 square foot facility in Novato, California used primarily for corporate, clinical, regulatory, manufacturing, and quality functions; and a 910 square foot facility in Novato, California used for research laboratory space. These leases expire in July 2016 and September 2014, respectively.

Legal Proceedings

We are not currently a party to any material legal proceedings.

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MANAGEMENT

Executive Officers, Directors, and Key Employees

The following table sets forth information regarding our executive officers, directors and nominee for director, and key employees as of January 10, 2014:

Name	Age	Position(s)
Executive Officers		
Emil D. Kakkis, M.D., Ph.D.	53	President and Chief Executive Officer, Director
Thomas Kassberg	53	Chief Business Officer and Senior Vice President
Shalini Sharp	38	Chief Financial Officer and Senior Vice President
Non-Employee Directors and Director Nominees		
Eran Nadav, Ph.D.	44	Chairman of the Board
William Aliski	66	Director
Benjamin Auspitz[(1)]	40	Director
Mårten Steen, M.D., Ph.D.	38	Director
Matthew K. Fust[(2)]	49	Director nominee
Clay B. Siegall, Ph.D.[(2)]	53	Director nominee
Key Employees		
Michael P. Cohrs, Ph.D.	52	Vice President of Quality
John Ditton	49	Vice President, Commercial Planning
Steven Jungles	48	Senior Vice President, Technical Operations
Tony Koutsoukos, Ph.D.	53	Vice President, Biometrics
Cordelia Leonard, RAC	53	Vice President, Regulatory Affairs and Quality Assurance
Javier San Martin, M.D.	48	Vice President, Clinical Development
Vimal Srivastava	48	Vice President, Program Development
Michael Vellard, Ph.D.	52	Vice President, Research
Spencer Guthrie	38	Senior Director, Clinical Operations
Alison Skrinar	43	Senior Director, Clinical Sciences

(1) Mr. Auspitz will resign from our board of directors immediately prior to the declaration of effectiveness of the registration statement of which this prospectus forms a part.

(2) We expect that this individual will become a member of our board of directors upon the declaration of effectiveness of the registration statement of which this prospectus forms a part.

Executive Officers

Emil D. Kakkis, M.D., Ph.D. is our founder and has served as our President and Chief Executive Officer and as a member of our board of directors since inception in April 2010. Prior to Ultragenyx, Dr. Kakkis served from September 1998 to February 2009 in various executive capacities, and ultimately as Chief Medical Officer, at BioMarin Pharmaceutical Inc., a biopharmaceutical company. Dr. Kakkis also serves as President and Founder of EveryLife Foundation for Rare Diseases, a non-profit organization he started in 2009 to accelerate biotechnology innovation for rare diseases. Dr. Kakkis is board certified in both Pediatrics and Medical Genetics. He holds a B.A. in Biology from Pomona College and received combined M.D. and Ph.D. degrees from the UCLA School of Medicine s Medical Scientist Training Program and received the Bogen prize for his research. We believe that Dr. Kakkis possesses specific expert knowledge of genetics and rare diseases that qualifies him to serve on our board of directors, including his leadership, management, and operational experience in the life sciences sector.

Thomas Kassberg has served as our Chief Business Officer and Senior Vice President since November 2011. Prior to Ultragenyx, Mr. Kassberg worked as Vice President of Business Development at Corium International, Inc., a biotechnology company, from July 2010 until October 2011. Prior to his work at Corium International, Inc., Mr. Kassberg worked as an independent consultant in Corporate Development and Business Strategy and consulted with a number of companies from March 2009 to June 2010, including Corium

International, Inc. and Rib-X Pharmaceuticals, Inc., a pharmaceutical company focused on the development of

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novel antibiotics. Before becoming a consultant, Mr. Kassberg worked at Proteolix, Inc., a biotechnology company subsequently acquired by Onyx Pharmaceuticals, from January 2008 until February 2009, where he served as Senior Vice President of Corporate Development. Mr. Kassberg holds a B.A. in Business Administration from Gustavus Adolphus College and an M.B.A. from Northwestern University.

Shalini Sharp has served as our Chief Financial Officer and Senior Vice President since May 2012. Prior to Ultragenyx, Ms. Sharp served in various executive capacities, and ultimately as Chief Financial Officer, of Agenus Inc., a biotechnology company, from August 2003 until May 2012. Prior to Agenus, Ms. Sharp held strategic planning and corporate finance roles and ultimately served as chief of staff to the chairman of the board at Elan Pharmaceuticals, a biotechnology company, from August 1998 to August 1999 and September 2001 to August 2003. Prior to Elan, Ms. Sharp was a management consultant at McKinsey & Company and an investment banker at Goldman Sachs, specializing in pharmaceuticals and medical devices. Ms. Sharp has also served as a board member of Agenus since May 2012. Ms. Sharp holds a B.A. and an M.B.A. from Harvard University.

Non-Employee Directors

Eran Nadav, Ph.D. has served as a member of our board of directors since June 2011 and has served as our Chairman of the board since January 2012. Dr. Nadav is a Managing Director at TPG Biotech®, the life science venture investment arm of TPG, a global private investment firm. Dr. Nadav joined TPG in 2007 with a focus on global pharmaceuticals and biotechnology investments. Prior to TPG, Dr. Nadav served as Business Development Director at Eisai, a pharmaceutical company, from September 2003 to August 2007 and also as a manager at Johnson & Johnson Development Corporation, the venture capital arm of Johnson & Johnson, a healthcare company, from November 1999 until July 2002. Dr. Nadav served on the board of directors of Eden Springs Ltd., a European provider of drinking water solutions for the workplace, from July 2010 until August 2011. Since June 2013 he has been serving on the board of directors of MacroGenics, Inc., a biopharmaceutical company. Dr. Nadav received a B.Sc. magna cum laude in Life Sciences, an M.Sc. magna cum laude and Ph.D. in Biochemistry, as well as an M.B.A., from Tel Aviv University. We believe that Dr. Nadav is qualified to serve on our board of directors due to his experience in the venture capital industry and his years of analyzing development opportunities in the life sciences sector.

William Aliski has served as a member of our board of directors since January 2011. Mr. Aliski served as a commercial consultant for early stage orphan disease companies, including Enobia Pharma, from September 2011 until March 2012. Before that, Mr. Aliski served as Senior Vice President and Chief Commercial Officer of FoldRx Pharmaceuticals, a rare disease company that is now a wholly-owned subsidiary of Pfizer Inc., from June 2009 until March 2011, as Director of Simon Kucher Partners, a global consulting firm, from January 2008 until June 2009 and as General Manager of BioMarin Europe at BioMarin Pharmaceuticals Inc. from December 2005 until January 2008. Mr. Aliski received a B.S. in Economics and a Master of Social Planning from Boston College and an M.P.A. from the Kennedy School of Government at Harvard University. We believe that Mr. Aliski is qualified to serve on our board of directors due to his extensive experience in the life sciences industry, membership of various boards of directors, and his leadership and management experience.

Benjamin Auspitz has served as a member of our board of directors since June 2011. Mr. Auspitz has served as a Partner at Fidelity Biosciences, a venture capital firm, since November 2005. Mr. Auspitz received a B.A. in Philosophy from Harvard University. We believe that Mr. Auspitz is qualified to serve on our board of directors due to his experience in the venture capital industry, membership of various other boards of directors, and his leadership and management experience.

Mårten Steen, M.D., Ph.D. has served as a member of our board of directors since June 2011. Dr. Steen has served as a Partner at HealthCap, a private equity firm, since March 2010. Prior to HealthCap, Dr. Steen served as Associate Director at Merck Serono, a biopharmaceutical company, from February 2008 until March 2010. Dr. Steen received a B.Sc. in Business Administration, an M.D. and a Ph.D. in Clinical Chemistry from Lund University. We believe that Dr. Steen is qualified to serve on our board of directors due to his medical and scientific background as well as his experience in the venture capital industry.

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Matthew K. Fust joined us as a board observer in November 2013 and is expected to become a member of our board of directors upon the declaration of effectiveness of the registration statement of which this prospectus forms a part. Mr. Fust currently serves as Executive Vice President of Onyx Pharmaceuticals, Inc., a biopharmaceutical company that was recently acquired by Amgen, Inc., and has served in this position since January 2009. From May 2003 to December 2008, Mr. Fust served as Chief Financial Officer at Jazz Pharmaceuticals, Inc., a specialty pharmaceutical company. From 2002 to 2003, Mr. Fust served as Chief Financial Officer at Perlegen Sciences, a biopharmaceutical company. Previously, he was Senior Vice President and Chief Financial Officer at ALZA Corporation, a pharmaceutical company, where he was an executive from 1996 until 2002. From 1991 until 1996, Mr. Fust was a manager in the healthcare strategy practice at Andersen Consulting. Mr. Fust serves on the Board of Directors of Sunesis Pharmaceuticals, Inc., a biopharmaceutical company. Mr. Fust received a B.A. from the University of Minnesota and an M.B.A. from the Stanford Graduate School of Business. We believe that Mr. Fust is qualified to serve on our board of directors due to his extensive experience in the life sciences industry, his leadership and management experience, and his service as a director of another public biopharmaceutical company.

Clay B. Siegall, Ph.D. joined us as a board observer in January 2014 and is expected to become a member of our board of directors upon the declaration of effectiveness of the registration statement of which this prospectus forms a part. Dr. Siegall currently serves as President and Chief Executive Officer and Chairman of the Board of Seattle Genetics, Inc., a biotechnology company. Dr. Siegall co-founded Seattle Genetics in 1998. Prior to Seattle Genetics, Dr. Siegall worked for the Bristol-Myers Squibb Pharmaceutical Research Institute from 1991 to 1997 and the National Cancer Institute, National Institutes of Health from 1988 to 1991. In addition to Seattle Genetics, Dr. Siegall serves as a director of Alder BioPharmaceuticals, Inc., a privately-held biotechnology company and Mirna Therapeutics, Inc., a privately-held biotechnology company. Dr. Siegall received a B.S. in Zoology from the University of Maryland and a Ph.D. in Genetics from George Washington University. We believe that Dr. Siegall is qualified to serve on our board of directors due to his extensive experience in the life sciences industry and his leadership and management experience.

Key Employees

Michael P. Cohrs, Ph.D. has served as our Vice President of Quality since December 2013 and is responsible for overseeing our GMP, GLP, GCP, and Clinical Assay departments. Prior to Ultragenyx, Dr. Cohrs served as Senior Director of Quality Assurance/Quality Control at Medicines 360, a pharmaceutical company, from October 2012 through November 2013 and previously served as the Director of Quality Assurance at Medicines 360 from September 2009 through October 2012. Prior to Medicines 360, Dr. Cohrs served as the Director of Quality Assurance at Sunesis Pharmaceuticals Inc., a pharmaceutical company, from June 2007 to June 2008. Dr. Cohrs has also held increasingly responsible positions at a number of large pharmaceutical and small start-up companies, first in Quality Control and then in Quality Assurance, including Aventis Behring, Genetics Institute, Chiron, and InterMune. Dr. Cohrs has also contributed to numerous regulatory submissions resulting in several product approvals in both the United States and Europe. Dr. Cohrs received his Ph.D. in Organic Chemistry from Washington University and an M.B.A. in International Business from the University of Chicago.

John Ditton has served as our Vice President, Commercial Planning since April 2011. Prior to Ultragenyx, Mr. Ditton was the Chief Operating Officer at EveryLife Foundation for Rare Diseases, from January 2009 to April 2011. Prior to working at the EveryLife Foundation, Mr. Ditton served as the Vice President of Marketing at Diamics, Inc., a maker of cancer diagnostics, from October 2006 to December 2008 and Director of Global Marketing at BioMarin Pharmaceutical Inc., a biopharmaceutical company, from March 2004 to March 2006. Mr. Ditton holds an M.B.A. from the University of Tasmania.

Steven Jungles has served as our Senior Vice President, Technical Operations since August 2011. Prior to Ultragenyx, Mr. Jungles worked as Vice President, Supply Chain at BioMarin Pharmaceutical Inc., a biopharmaceutical company, from June 1999 to July 2011, was Associate Director of Operations at Harvard Gene Therapy Initiative from June 1997 until June 1999, and worked at Somatix Therapy Corporation, a research and development company in the field of gene therapy that was acquired by Cell Genesys, Inc., from March 1993 to May 1997. Mr. Jungles holds a B.S. in Biology from the University of Iowa.

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Tony Koutsoukos, Ph.D. has served as our Vice President of Biometrics since October 2013. Prior to Ultragenyx, Mr. Koutsoukos worked as Vice President of Biometrics at Allos Therapeutics, a biopharmaceutical company, from September 2007 to March 2013, which was acquired by Spectrum Pharmaceuticals. He was also Director of Biostatistics at Amgen Inc., a biotechnology company, from May 2002 to September 2007. Prior to Amgen, Mr. Koutsoukos spent three years at Quintiles, a contract research company, as a Director of Biostatistics. His experience also includes five years at the FDA, Center for Drugs Evaluation and Research (CDER) division and approximately four years at the National Cancer Institute, Biometric Research Branch, CTEP, DCT. Dr. Koutsoukos received his Ph.D. and M.A., both in Mathematical Statistics from the University of Maryland, College Park.

Cordelia Leonard has served as our Vice President, Regulatory Affairs and Quality Assurance since July 2011. Prior to Ultragenyx, Ms. Leonard was Senior Director, Regulatory Affairs at BioMarin Pharmaceutical Inc., a biopharmaceutical company, from October 2003 until July 2011. Prior to BioMarin, Ms. Leonard was the Manager, Regulatory Affairs at Cerus Corporation, a biomedical products company, from May 1999 until October 2003. Ms. Leonard received bachelor degrees in Chemistry and Biological Science from the University of California, Irvine and holds both U.S. and EU Regulatory Affairs Certifications.

Javier San Martin, M.D. has served as our Vice President, Clinical Development since December 2013. Prior to Ultragenyx, Dr. San Martin served as Senior Vice President of Clinical Development at Alder Biopharmaceuticals Inc., a pharmaceutical company, from January 2012 through May 2013. Prior to Alder, Dr. San Martin served as Executive Director and Global Development Leader at Amgen, Inc., a biotechnology company, from March 2006 to September 2011. Prior to Amgen, Dr. San Martin served as Medical Advisor at Eli Lilly and Company, a pharmaceutical company, from June 1998 to February 2006. Dr. San Martin received his M.D. from the University of Buenos Aires Medical School and completed his residence in internal medicine at CEMIC University of Buenos Aires.

Vimal Srivastava has served as our Vice President, Program Development since August 2011. Before joining Ultragenyx, Mr. Srivastava was Senior Director, Portfolio and Project Management at Elan/Janssen Alzheimer Immunotherapy, a biotechnology company, from January 2008 until August 2011. He was also Director, Global Program Manager, Diabetes at Amgen Inc., a biotechnology company, from September 2005 to January 2008 and Director, Program Management at BioMarin Pharmaceutical Inc., a biopharmaceutical company, from March 2003 to September 2005. Mr. Srivastava holds a B.S. in Pharmacy from Banaras Hindu University, an M.S. in Medicinal Chemistry from St. John s University and an M.A.S. in Management from Johns Hopkins University.

Michael Vellard, Ph.D. has served as our Vice President, Research since May 2013. Prior to joining Ultragenyx, Dr. Vellard worked as Head of Lysosomal Biology at BioMarin Pharmaceutical Inc., a biopharmaceutical company, from October 1999 to May 2013. He was a postdoctoral fellow in the pediatric department at UCLA Harbor Medical Center from September 1992 to June 1995. Dr. Vellard received his B.S. in Natural and Life Sciences and M.S. in Molecular and Cellular Genetics from the University of Lyon I, France. He obtained his Ph.D. in Virology from the Pasteur and Curie Institutes (Universities Paris VI, VII and XI), France.

Spencer Guthrie has served as our Senior Director, Clinical Operations since June 2012. Prior to Ultragenyx, Mr. Guthrie worked as Director of Clinical Operations and Project Team Leader at Elan Pharmaceuticals, a biotechnology company, and Janssen Alzheimer s Immunotherapy from September 2007 to June 2012. Prior to that, Mr. Guthrie spent nine years with increasing responsibilities at Genentech in Clinical Operations and Market Planning. At Genentech, he worked on several innovative clinical programs, IND and BLA filings with Rituxan, Avastin, and Lucentis, including work on orphan indications. Mr. Guthrie also spent two years at ICON Clinical Research and a year at NASA s space science lab. Mr. Guthrie received his B.A. in Neuroscience from Vanderbilt University, an M.B.A. from the University of California, Irvine and he is certified as a Project Management Professional.

Alison Skrinar, Ph.D. has served as our Senior Director, Clinical Sciences since March 2012. Prior to joining Ultragenyx, Dr. Skrinar worked as the Senior Director of Clinical Outcomes and Regulatory Affairs from February 2009 to February 2012 at Enobia Pharma, Inc., a private clinical stage orphan company focused on the

development of an enzyme replacement therapy for hypophosphastasia, which was acquired by Alexion in 2012. Prior to Enobia Pharma, Dr. Skrinar was the Senior Director of Clinical Outcomes at Genzyme Corporation, a biotechnology company, from May 2001 until January 2009. In her nearly 15 years in the biotechnology industry, Dr. Skrinar has worked exclusively on the clinical development and regulatory approval of ultra-orphan drugs. Dr. Skrinar received a B.B.A. from Emory University and a Ph.D. and a Master of Public Health degree from the University of Alabama.

Board Composition

Director Independence

Our board of directors currently consists of five members and we anticipate that it will consist of six members upon the declaration of effectiveness of the registration statement of which this prospectus forms a part. Our board of directors has determined that all of our directors, other than Dr. Kakkis, and both of our director nominees, qualify as independent directors in accordance with the NASDAQ listing requirements. Dr. Kakkis is not considered independent because he is an employee of Ultragenyx. The NASDAQ independence definition includes a series of objective tests, such as that the director is not, and has not been for at least three years, one of our employees and that neither the director nor any of his family members has engaged in various types of business dealings with us. In addition, as required by NASDAQ rules, our board of directors has made a subjective determination as to each independent director and director nominee that no relationships exist, which, in the opinion of our board of directors, would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In making these determinations, our board of directors reviewed and discussed information provided by the directors, director nominees, and us with regard to each director s and director nominee s business and personal activities and relationships as they may relate to us and our management. There are no family relationships among any of our directors or executive officers.

Classified Board of Directors

We currently have five directors, all of whom were elected pursuant to the terms of a voting agreement by and among us and certain of our stockholders, which will terminate upon completion of this offering. Upon the termination of the voting agreement, we will not be bound by contractual obligations regarding the election of our directors.

Effective upon the declaration of effectiveness of the registration statement of which this prospectus forms a part, we anticipate that we will have six directors and will divide the terms of office of the directors into three classes:

Class I, whose term will expire at the annual meeting of stockholders to be held in 2014;

Class II, whose term will expire at the annual meeting of stockholders to be held in 2015; and

Class III, whose term will expire at the annual meeting of stockholders to be held in 2016.

Upon the declaration of effectiveness of the registration statement of which this prospectus forms a part, Class I shall consist of Emil D. Kakkis and Mårten Steen, Class II is expected to consist of Eran Nadav and Clay Siegall, and Class III is expected to consist of Matthew Fust and William Aliski. Benjamin Auspitz, currently a member of our board of directors, has indicated to us his intention to resign from our board of directors immediately prior to the declaration of effectiveness of the registration statement of which this prospectus forms a part. At each annual meeting of stockholders after the initial classification, the successors to directors whose terms will then expire shall serve from the time of election and qualification until the third annual meeting following election and until their successors are duly elected and qualified. A resolution of the board of directors may change the authorized number of directors. Any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class will consist of one-third of the directors. This classification of the board of directors may have the effect of delaying or preventing changes in control or management of our company.

Following the completion of this offering, our nominating and corporate governance committee and board of directors may consider a broad range of factors relating to the qualifications and background of nominees, which may include diversity and is not limited to race, gender, or national origin. We have no formal policy regarding board diversity. Our nominating and corporate governance committee s and board of directors priority in selecting

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board members is identification of persons who will further the interests of our company through his or her established record of professional accomplishment, the ability to contribute positively to the collaborative culture among board members, and professional and personal experiences and expertise relevant to our growth strategy.

Board Committees

Effective upon the completion of this offering, our board of directors will have three standing committees: the audit committee, the compensation committee and the nominating and corporate governance committee.

Audit Committee

Effective upon the declaration of effectiveness of the registration statement of which this prospectus forms a part, our audit committee is expected to consist of Eran Nadav, Matthew Fust and Mårten Steen, with Matthew Fust serving as chairman of the committee. Our board of directors has determined that each member of the audit committee meets the independence requirements of Rule 10A-3 under the Exchange Act and the applicable listing standards of NASDAQ. Our board of directors has determined that Matthew Fust is an audit committee financial expert within the meaning of the SEC regulations and applicable listing standards of NASDAQ. The audit committee s responsibilities upon completion of this offering will include:

- appointing, approving the compensation of, reviewing the performance of, and assessing the independence of our independent registered public accounting firm;
- approving audit and permissible non-audit services, and the terms of such services, to be provided by our independent registered public accounting firm;
- reviewing the audit plan with the independent registered public accounting firm and members of management responsible for preparing our financial statements;
- reviewing and discussing with management and the independent registered public accounting firm our annual and quarterly financial statements and related disclosures as well as critical accounting policies and practices used by us;
- reviewing the adequacy of our internal control over financial reporting;
- establishing policies and procedures for the receipt and retention of accounting-related complaints and concerns;
- recommending, based upon its review and discussions with management and the independent registered public accounting firm, whether our audited financial statements shall be included in our Annual Report on Form 10-K;
- preparing the audit committee report required by the rules of the SEC to be included in our annual proxy statement;
- reviewing all related party transactions for potential conflict of interest situations and approving all such transactions;
- reviewing policies related to risk assessment and risk management; and

establishing, maintaining and overseeing our Code of Business Conduct and Ethics.

Compensation Committee

Effective upon the declaration of effectiveness of the registration statement of which this prospectus forms a part, our compensation committee is expected to consist of Eran Nadav, William Aliski, and Clay Siegall, with Eran Nadav serving as chairman of the committee. Our board of directors has determined each member of the compensation committee is independent as defined under the applicable listing standards of NASDAQ. The compensation committee s responsibilities upon completion of this offering will include:

annually reviewing and approving individual and corporate goals and objectives relevant to the compensation of our executive officers;

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evaluating the performance of our executive officers in light of such individual and corporate goals and objectives and determining the compensation of our executive officers;

appointing, compensating and overseeing the work of any compensation consultant, legal counsel or other advisor retained by the compensation committee;

conducting the independence assessment outlined in NASDAQ rules with respect to any compensation consultant, legal counsel, or other advisor retained by the compensation committee;

annually reviewing and reassessing the adequacy of the committee charter in its compliance with the listing requirements of NASDAQ;

overseeing and administering our compensation and similar plans;

reviewing and approving our policies and procedures for the grant of equity-based awards;

reviewing and making recommendations to the board of directors with respect to director compensation;

reviewing and discussing with management the compensation discussion and analysis, if any, to be included in our annual proxy statement or Annual Report on Form 10-K;

preparing the compensation committee report required by the rules of the SEC to be included in our annual proxy statement; and

reviewing and discussing with the board of directors corporate succession plans for the chief executive officer and other senior management positions.

Nominating and Corporate Governance Committee

Effective upon the declaration of effectiveness of the registration statement of which this prospectus forms a part, our nominating and corporate governance committee is expected to consist of Matthew Fust, Eran Nadav and Mårten Steen, with Matthew Fust serving as chairman of the committee. Our board of directors has determined that each member of the nominating and corporate governance committee is independent as defined under the applicable listing standards of NASDAQ. The nominating and corporate governance committee s responsibilities upon completion of this offering will include:

developing and recommending to the board of directors criteria for board and committee membership;

establishing procedures for identifying and evaluating board of director candidates, including nominees recommended by stockholders;

identifying individuals qualified to become members of the board of directors;

recommending to the board of directors the persons to be nominated for election as directors and to each of the board s committees; and

developing and recommending to the board of directors a set of corporate governance guidelines.

Our board of directors may establish other committees from time to time.

Leadership Structure and Risk Oversight

Our board of directors is currently chaired by Dr. Nadav. As a general policy, our board of directors believes that separation of the positions of chairman and chief executive officer reinforces the independence of the board of directors from management, creates an environment that encourages objective oversight of management s performance and enhances the effectiveness of the board of directors as a whole. As such, Dr. Kakkis serves as our president and chief executive officer while Dr. Nadav serves as our chairman of the board of directors but is not an officer.

Our board of directors oversees the management of risks inherent in the operation of our business and the implementation of our business strategies. Our board of directors performs this oversight role by using several different levels of review. In connection with its reviews of the operations and corporate functions of our company, our board of directors addresses the primary risks associated with those operations and corporate

functions. In addition, our board of directors reviews the risks associated with our company s business strategies periodically throughout the year as part of its consideration of undertaking any such business strategies.

Each of our board committees also oversees the management of our company s risk that falls within the committee s areas of responsibility. In performing this function, each committee has full access to management, as well as the ability to engage advisors. Our chief financial officer reports to the audit committee and is responsible for identifying, evaluating, and implementing risk management controls and methodologies to address any identified risks. In connection with its risk management role, our audit committee meets privately with representatives from our independent registered public accounting firm. The audit committee oversees the operation of our risk management program, including the identification of the primary risks associated with our business and periodic updates to such risks, and reports to our board of directors regarding these activities.

Compensation Committee Interlocks and Insider Participation

None of the members of our compensation committee has at any time during the prior three years been one of our officers or employees. None of our executive officers currently serves, or in the past fiscal year has served, as a member of the board of directors or compensation committee of any entity that has one or more executive officers serving on our board of directors or compensation committee. For a description of transactions between us and members of our compensation committee and affiliates of such members, please see Certain Relationships and Related Party Transactions.

Board Diversity

Effective upon the completion of this offering, our nominating and corporate governance committee will be responsible for reviewing with the board of directors, on an annual basis, the appropriate characteristics, skills and experience required for the board of directors as a whole and its individual members. Although we do not have a formal policy regarding board diversity, in evaluating the suitability of individual candidates (both new candidates and current members), the nominating and corporate governance committee, in recommending candidates for election, and the board of directors, in approving (and, in the case of vacancies, appointing) such candidates, will take into account many factors, including the following:

- personal and professional integrity;
- ethics and values;
- experience in corporate management, such as serving as an officer or former officer of a publicly held company;
- experience in the industries in which we compete;
- experience as a board member or executive officer of another publicly held company;
- diversity of expertise and experience in substantive matters pertaining to our business relative to other board members;
- conflicts of interest; and
- practical and mature business judgment.

Currently, our board of directors evaluates, and, following the completion of this offering will evaluate, each individual in the context of the board of directors as a whole, with the objective of assembling a group that can best maximize the success of the business and represent stockholder interests through the exercise of sound judgment using its diversity of experience in these various areas.

Code of Business Conduct and Ethics

We have adopted a code of business conduct and ethics that applies to all of our employees, officers, and directors, including those officers responsible for financial reporting. Upon the completion of this offering, our code of business conduct and ethics will be available on our website. We intend to disclose any amendments to the code, or any waivers of its requirements, on our website.

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EXECUTIVE AND DIRECTOR COMPENSATION

The following is a summary of the compensation arrangements of our named executive officers. Actual compensation programs that we may adopt may differ materially from currently planned programs as summarized in this discussion. As an emerging growth company as defined in the JOBS Act, we are not required to include a Compensation Discussion and Analysis section and have elected to comply with the scaled disclosure requirements applicable to emerging growth companies.

Summary Compensation Table

The following table sets forth the compensation earned during the years ended December 31, 2013 and 2012 to our chief executive officer and our next two highest-paid executive officers. We refer to these officers as our named executive officers.

Name and Principal Position	Year	Salary	Bonus	Option Awards[1]	Nonequity Incentive Plan Compensation[2]	All Other Compensation	Total
Emil D. Kakkis, M.D., Ph.D.	2013	$ 306,034		$ 218,873		$ 19,721	$ 544,628
President and Chief Executive Officer	2012	$ 300,172			$ 92,125	$ 9,056[3]	$ 401,353
Thomas Kassberg	2013	$ 289,419		$ 182,394		$ 20,352	$ 492,165
Chief Business Officer and Senior Vice President	2012	$ 272,041			$ 81,813	$ 15,640[4]	$ 369,494
Shalini Sharp[5]	2013	$ 278,440	$ 30,000	$ 182,394		$ 24,193	$ 515,027
Chief Financial Officer and Senior Vice President	2012	$ 148,669		$ 90,042	$ 51,560	$ 13,228[4]	$ 303,499

(1) The amounts reported in this column represent the grant date fair value of the stock options granted to our named executive officers during 2013 and 2012, respectively, as computed in accordance with Accounting Standards Codification, or ASC, Topic 718, not including any estimates of forfeitures. The assumptions used in calculating the grant date fair value of the stock options reported in this column are set forth in the notes to our financial statements included elsewhere in this prospectus. Note that the amounts reported in this column reflect the accounting cost for these stock options, and do not correspond to the actual economic value that may be received by the named executive officers from the options.

(2) Cash bonuses earned in fiscal 2013, which will be based on achievement of performance goals and other factors deemed relevant by our board of directors, have not yet been determined as of the date of this prospectus. Amounts for fiscal 2012 represent cash bonuses earned in 2012, and paid during 2013, based on achievement of performance goals and other factors deemed relevant by our board of directors.

(3) Amounts reported in this column consist of medical, dental, vision and life/accidental death & dismemberment and key person life insurance premiums paid by us.

(4) Amounts reported in this column consist of medical, dental, vision and life/accidental death & dismemberment premiums paid by us.

(5) Ms. Sharp commenced employment with us in May 2012.

Narrative Disclosure to Summary Compensation Table

Employment Arrangements with Our Named Executive Officers

Emil D. Kakkis, M.D., Ph.D., President and Chief Executive Officer. We entered into an executive employment agreement with Dr. Kakkis in June 2011 for the position of President and Chief Executive Officer.

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Dr. Kakkis currently receives a base salary of $305,000, which is subject to adjustment at the discretion of the board of directors or the compensation committee. Dr. Kakkis is also eligible to participate in our employee benefit plans, subject to the terms of those plans. Pursuant to the terms of the executive employment agreement, the employment of Dr. Kakkis is at will; we may terminate his employment at any time, without advance notice, for any reason or for no reason at all and Dr. Kakkis may terminate his employment at any time, upon four weeks prior written notice, for any reason or for no reason at all.

Thomas Kassberg, Chief Business Officer and Senior Vice President. We entered into an offer letter in October 2011 with Thomas Kassberg for the position of Chief Business Officer and Senior Vice President. Mr. Kassberg currently receives a base salary of $288,750, which is subject to adjustment at the discretion of the board of directors or the compensation committee. Mr. Kassberg is also eligible for an annual performance bonus of up to 30% of his base salary, payable based on his individual performance evaluated against certain goals mutually agreed upon and our overall performance, as determined by the Chief Executive Officer in consultation with the board of directors. Additionally, pursuant to the terms of the offer letter, Mr. Kassberg received an option to purchase 202,584 shares of our common stock in connection with his hiring. Mr. Kassberg is eligible to participate in our employee benefit plans, subject to the terms of those plans. Pursuant to the terms of the offer letter, Mr. Kassberg s employment is at will and may be terminated either by us or by him, with or without advance notice, for any reason or for no reason at all.

Shalini Sharp, Chief Financial Officer and Senior Vice President. We entered into an offer letter in March 2012 with Shalini Sharp for the position of Chief Financial Officer and Senior Vice President. Ms. Sharp currently receives a base salary of $278,299, which is subject to adjustment at the discretion of the board of directors or the compensation committee. Ms. Sharp is also eligible for an annual performance bonus of up to 30% of her base salary, payable based on her individual performance evaluated against certain goals mutually agreed upon and our overall performance, as determined by the Chief Executive Officer in consultation with the board of directors. Additionally, pursuant to the terms of the offer letter, Ms. Sharp received an option to purchase 191,418 shares of our common stock in connection with her hiring. Ms. Sharp is eligible to participate in our employee benefit plans, subject to the terms of those plans. Pursuant to the terms of the offer letter, Ms. Sharp s employment is at will and may be terminated either by us or by her, with or without advance notice, for any reason or for no reason at all.

Each of these employment arrangements also contain provisions that provide for certain payments and benefits in the event of an involuntary termination of employment. In addition, the named executive officers may be entitled to accelerated vesting of their outstanding and unvested awards in certain circumstances. The information below describes certain compensation that may become due and payable as a result of certain events.

Involuntary Termination of Employment

Pursuant to their employment arrangements, each named executive officer is eligible to receive certain payments and benefits in the event of certain qualifying terminations, including termination of his or her employment by us without cause (as defined below) or resignation of his or her employment with good reason or because of a constructive termination (each, as defined below). Upon the timely execution of a general release of claims, each named executive officer is eligible to receive the following payments and benefits:

- if Dr. Kakkis is terminated by us other than for cause or because of death or disability, he shall be entitled to receive six months of base salary continuation;
- if Dr. Kakkis resigns his employment with us for good reason following a change in control (as defined below) within six months of the event constituting good reason and after providing us with 20 days to cure the good reason, then he shall be entitled to receive 12 months of base salary continuation; and
- if Mr. Kassberg or Ms. Sharp is terminated by us without cause or resigns employment with us due to a constructive termination, each executive will be entitled to: (i) extend the exercise period applicable to

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any options then held such that the executive has 12 months from termination to exercise any of the vested shares, provided that in no event shall the exercise period be extended beyond the expiration date of any options then held; and (ii) six months of base salary continuation.

Deemed Liquidation Event

Pursuant to the offer letter with Mr. Kassberg, in addition to the severance benefits described above, in the event (i) we consummate a deemed liquidation event (as defined in our certificate of incorporation), which includes certain mergers or material asset sales, as well as any dissolution, liquidation, or winding down of the Company, (ii) Mr. Kassberg is employed by us on the date of the deemed liquidation event, and (iii) Mr. Kassberg is terminated by us without cause or resigns his employment with us due to a constructive termination within 12 months after the deemed liquidation event, the vesting of Mr. Kassberg s November 17, 2011 option to purchase 202,584 shares of our common stock shall accelerate with respect to 50% of the then-unvested shares subject to such option and any other equity held by Mr. Kassberg shall accelerate with respect to 100% of the then-unvested shares.

Pursuant to the offer letter with Ms. Sharp, in the event (i) we consummate a deemed liquidation event, (ii) Ms. Sharp is employed by us on the date of the deemed liquidation event, and (iii) Ms. Sharp is terminated without cause or resigns due to a constructive termination within 12 months of the deemed liquidation event, the vesting of all options held by Ms. Sharp as of the date of the deemed liquidation event shall accelerate with respect to 50% of the then-unvested shares.

Definitions

For purposes of Dr. Kakkis s employment agreement, cause means his:

commission of a felony or any crime involving dishonesty, breach of trust, or physical harm to any person;

willful engagement in conduct that is in bad faith and materially injurious to us, including but not limited to misappropriation of trade secrets, fraud, or embezzlement;

material breach of his employment agreement that is not cured within 10 days after written notice to him from us; or

willful refusal to implement or follow a lawful policy or directive of ours, which breach is not cured within 10 days after written notice to him from us.

For purposes of each of the offer letters with Mr. Kassberg and Ms. Sharp, cause means the named executive officer s:

gross negligence in carrying out, or material failure to carry out, his or her duties for us (including, without limitation, failure to cooperate in any company investigation), after notice from the board of directors and a reasonable opportunity to cure (if deemed curable);

breach of his or her fiduciary duties to us, after notice from the board of directors and a reasonable opportunity to cure (if deemed curable);

conviction of, or plea of guilty or no contest to, any felony;

any act of fraud or embezzlement with respect to his or her obligations to us or otherwise relating to our business;

material violation of any of our policies;

material breach of any agreement entered into with us; or

unauthorized use or disclosure of confidential information or trade secrets of ours or of our affiliates.

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For purposes of Dr. Kakkis s employment agreement, good reason means any of the following events if (i) we effect the event without the consent of Dr. Kakkis and (ii) such event occurs after a change in control:

- a change in his position with us that materially reduces his level of responsibility;
- a material reduction in his base salary, except for reductions that are comparable to reductions generally applicable to similarly situated executives of ours; or
- a relocation of his principal place of employment by more than 50 miles.

For purposes of Dr. Kakkis s employment agreement, change in control means a change in ownership or control of us effected through a merger, consolidation, or acquisition by any person or related group of persons (other than an acquisition by us or by an employee benefit plan sponsored by us or by a person or persons that directly or indirectly control, is controlled by, or is under common control with, us) of beneficial ownership of securities possessing more than 50% of the total combined voting power of our outstanding securities.

For purposes of each of the offer letters with Mr. Kassberg and Ms. Sharp, constructive termination means the occurrence of any of the following events without the named executive officer s consent if (i) the executive provides us with written objection (or notice) to the event or condition within 30 days following the occurrence of the event or condition, (ii) we do not reverse or otherwise cure the event within 30 days of receiving such written objection, and (iii) the executive resigns his or her employment with us within 30 days following the expiration of that cure period:

- a material reduction or change in the executive s job duties, responsibilities and requirements from the executive s job duties, responsibilities and requirements immediately prior to such reduction or change, taking into account the differences in job title and duties that are normally occasioned by reason of an acquisition of one company by another;
- a material reduction of the executive s base salary (other than an equal, across-the-board reduction in the compensation of all similarly-situated employees of ours or the surviving entity that is approved by the board of directors); or
- a requirement that the executive relocate to a principal office that increases his or her one-way commute by more than 50 miles relative to the executive s immediately preceding principal office.

Terms and Conditions of Annual Bonuses

Our board of directors has adopted a corporate bonus plan, or the bonus plan, which is effective as of the completion of this offering. The bonus plan provides for cash bonus payments based upon the attainment of performance targets established by our compensation committee. The payment targets will be related to corporate, financial, and operational measures or objectives, or corporate performance goals, as well as individual performance objectives.

Our compensation committee may select corporate performance goals from among the following: sales; revenue; assets; expenses; earnings from operations, earnings before or after deduction for all or any portion of interest, taxes, depreciation, amortization, incentives, service fees or extraordinary or special items, whether or not on a continuing operations or an aggregate or per share basis; net income or net income per common share (basic or diluted); return on equity, investment, capital or assets; one or more operating ratios; borrowing levels, leverage ratios or credit rating; market share; capital expenditures; cash flow, free cash flow, cash flow return on investment, or net cash provided by operations; stock price, dividends or total stockholder return; development of new technologies or products; sales of particular products or services; economic value created or added; operating margin or profit margin; customer acquisition or retention; raising or refinancing of capital; successful hiring of key individuals; resolution of significant litigation; acquisitions and divestitures (in whole or in part); joint ventures and strategic alliances; spin-offs, split-ups and the like; reorganizations; recapitalizations, restructurings, financings (issuance of debt or equity) or refinancings; or strategic business criteria, consisting of one or more objectives based on the following goals: meeting specified market penetration or value added, product development or introduction (including, without limitation, any clinical trial accomplishments,

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regulatory or other filings or approvals, or other product development milestones), geographic business expansion, cost targets, cost reductions or savings, customer satisfaction, operating efficiency, acquisition or retention, employee satisfaction, information technology, corporate development (including, without limitation, licenses, innovation, research or establishment of third party collaborations), manufacturing or process development, legal compliance or risk reduction, patent application or issuance goals, or goals relating to acquisitions or divestitures (in whole or in part), joint ventures or strategic alliances, any of which may be measured in absolute terms, as compared to any incremental increase, in terms of growth, as compared to results of a peer group, against the market as a whole, compared to applicable market indices and/or measured on a pre-tax or post-tax basis.

Each executive officer who is selected to participate in the bonus plan will have a target bonus opportunity set for each performance period. The bonus formulas will be adopted in each performance period by the compensation committee and communicated to each executive. The corporate performance goals will be measured at the end of each performance period after our financial reports have been published or such other appropriate time as the compensation committee determines. If the corporate performance goals and individual performance objectives are met, payments will be made following the end of each performance period. Subject to the rights contained in any agreement between the executive officer and the company, an executive officer must be employed by the company on the bonus payment date to be eligible to receive a bonus payment. The bonus plan also permits the compensation committee to approve additional bonuses in its sole discretion.

Equity Compensation

Outstanding Equity Awards at December 31, 2013

The following table sets forth information concerning the outstanding equity awards held by each of the named executive officers as of December 31, 2013.

	Option awards			
Name	Number of securities underlying unexercised options (#) exercisable	Number of securities underlying unexercised options (#) unexercisable	Option exercise price ($)	Option expiration date
Emil D. Kakkis, M.D., Ph.D[(1)].		47,854	$ 6.86	10/31/2023
Thomas Kassberg[(2)]	12,661	97,071	0.31	11/16/2021
		39,878	$ 6.86	10/31/2023
Shalini Sharp[(3)]	11,963	115,648	0.81	8/1/2022
		39,878	$ 6.86	10/31/2023

(1) Represents an option to purchase 47,854 shares of our common stock granted on November 1, 2013. The shares underlying this option vest as follows: 25% vest on November 1, 2014, with the remainder of the shares vesting in equal monthly installments over the following three years through November 1, 2017, subject to the holder s continued service to us through each such vesting date.

(2) Represents an option to purchase 202,584 shares of our common stock granted on November 17, 2011. The shares underlying this option vest as follows: 25% vest on November 15, 2012, with the remainder of the shares vesting in equal monthly installments over the following three years through November 15, 2015, subject to the holder s continued service to us through each such vesting date. Vesting of 50% of the unvested shares shall accelerate in connection with a deemed liquidation event pursuant to the terms of Mr. Kassberg s offer letter dated October 31, 2011, as more fully described above under the section entitled Narrative Disclosure to Summary Compensation Table Deemed Liquidation Event. Mr. Kassberg exercised 50,646 options on November 28, 2012 and 42,204 options on September 27, 2013.

Represents an option to purchase 39,878 shares of our common stock granted on November 1, 2013. The shares underlying this option vest as follows: 25% vest on November 1, 2014, with the remainder of the

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shares vesting in equal monthly installments over the following three years through November 1, 2017, subject to the holder s continued service to us through each such vesting date.

(3) Represents an option to purchase 191,418 shares of our common stock granted on August 2, 2012. The shares underlying this option vest as follows: 25% vest on May 21, 2013, with the remainder of the shares vesting in equal monthly installments over the following three years through May 21, 2016, subject to the holder s continued service to us through each such vesting date. Vesting of 50% of the unvested shares shall accelerate in connection with a deemed liquidation event pursuant to the terms of Ms. Sharp s offer letter dated March 12, 2012, as more fully described above under the section entitled Narrative Disclosure to Summary Compensation Table Deemed Liquidation Event. Ms. Sharp exercised 47,854 options on May 30, 2013, 7,975 options on July 24, 2013, and 7,975 options on September 26, 2013. Represents an option to purchase 39,878 shares of our common stock granted on November 1, 2013. The shares underlying this option vest as follows: 25% vest on November 1, 2014, with the remainder of the shares vesting in equal monthly installments over the following three years through November 1, 2017, subject to the holder s continued service to us through each such vesting date.

Director Compensation

Dr. Kakkis, our president and chief executive officer, receives no compensation for his service as a director. None of our non-employee directors received compensation for their service on the board or otherwise during fiscal 2012.

Our board of directors has adopted a non-employee director compensation policy, effective as of the closing of this offering, that is designed to provide a total compensation package that enables us to attract and retain, on a long-term basis, high caliber non-employee directors. Under the policy, all non-employee directors will be paid cash compensation from and after the completion of this offering, as set forth below:

	Annual Retainer
Board of Directors:	
All non-employee members	$ 35,000
Audit Committee:	
Chairman	$ 15,000
Non-Chairman members	$ 7,500
Compensation Committee:	
Chairman	$ 10,000
Non-Chairman members	$ 5,000
Nominating and Corporate Governance Committee:	
Chairman	$ 6,000
Non-Chairman members	$ 3,000

Under the non-employee director compensation policy, each non-employee director serving on our board of directors upon the declaration of effectiveness of the registration statement of which this prospectus forms a part and each non-employee director who is initially appointed or elected to the board of directors after the completion of this offering will receive for an option grant to purchase up to 17,500 shares of our common stock under our stock option plan on the date he or she first becomes a non-employee director, which will vest annually over a three-year period, subject to the holder s continued service to us through each such vesting date. In addition, on the date of the annual meeting of stockholders, each continuing non-employee director will be eligible to receive an annual option grant to purchase up to 7,500 shares of our common stock, which will vest in full upon the first anniversary of the date of grant, subject to the holder s continued service to us through such vesting date. All of the foregoing options will be granted at fair market value on the date of grant.

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Compensation Risk Assessment

We believe that our executive compensation program does not encourage excessive or unnecessary risk taking. This is primarily due to the fact that our compensation programs are designed to encourage our executive officers and other employees to remain focused on both short-term and long-term strategic goals, in particular in connection with our pay-for-performance compensation philosophy. As a result, we do not believe that our compensation programs are reasonably likely to have a material adverse effect on us.

Equity Compensation Plans and Other Benefit Plans

2014 Incentive Plan

Prior to the completion of this offering, our board of directors intends to adopt the Ultragenyx Pharmaceutical Inc. 2014 Incentive Plan, or the 2014 Plan, and, following this offering, all equity-based awards will be granted under the 2014 Plan. As of the date of this prospectus, no awards have been made under the 2014 Plan. The following summary describes what we anticipate to be the material terms of the 2014 Plan. This summary of the 2014 Plan is not a complete description of all provisions of the 2014 Plan and is qualified in its entirety by reference to the 2014 Plan, which is filed as an exhibit to the registration statement of which this prospectus is a part.

Purpose. The purpose of the 2014 Plan is to advance the company s interests by providing for the grant to participants of equity and other incentive awards.

Plan Administration. The 2014 Plan is administered by our compensation committee. Our compensation committee has the authority to, among other things, interpret the 2014 Plan, determine eligibility for, grant and determine the terms of awards under the 2014 Plan, and to do all things necessary to carry out the purposes of the 2014 Plan. Our compensation committee s determinations under the 2014 Plan are conclusive and binding.

Authorized Shares. Subject to adjustment, the maximum number of shares of our common stock that may be delivered in satisfaction of awards under the 2014 Plan is 2,250,000, which includes the shares of our common stock that are available for grant under the 2011 Plan (defined and described below) on the date the 2014 Plan is adopted, and any shares that become available under the 2011 Plan as a result of the termination, cancellation or forfeiture of awards under the 2011 Plan. The number of shares of our common stock available for issuance under the 2014 Plan will be automatically increased on January 1 of each year, beginning January 1, 2015 through January 1, 2024, by an amount equal to the least of (i) 2,500,000 shares of common stock, (ii) 4% of the number of shares of common stock outstanding on a fully diluted basis as of the close of business on the immediately preceding day (calculated by adding to the number of shares of common stock outstanding, all outstanding securities convertible into common stock on such date on an as converted basis), and (iii) a lesser amount determined by the compensation committee on or prior to January 1 of a given year.

Shares of our common stock to be issued under the 2014 Plan may be authorized but unissued shares of our common stock or previously issued shares acquired by us. Any shares of our common stock underlying awards that are settled in cash or otherwise expire, terminate, or are forfeited prior to the issuance of stock will again be available for issuance under the 2014 Plan.

Individual Limits. The maximum number of shares of our common stock subject to stock options and the maximum number of shares of our common stock subject to stock appreciation rights that may be granted to any person in any calendar year is each 1,000,000 shares. The maximum number of shares of our common stock subject to other awards that may be granted to any person in any calendar year is 1,000,000 shares. The maximum amount payable to any person in any twelve-month period under cash awards will be $430,000. Any awards granted in excess of the foregoing limits will not be eligible to be excluded from the applicable Section 162(m) limits and such excess amount may not be deductible by the Company as performance-based compensation.

Eligibility. Our compensation committee will select participants from among our key employees, directors, consultants and advisors and of our affiliates who are in a position to contribute significantly to the success of the company and its affiliates. Eligibility for options intended to be incentive stock options, or ISOs, is limited to employees of the company or certain affiliates.

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Types of Awards. The 2014 Plan provides for grants of stock options, stock appreciation rights, restricted and unrestricted stock and stock units, performance awards, cash awards and other awards convertible into or otherwise based on shares of our common stock. Dividend equivalents may also be provided in connection with an award under the 2014 Plan.

Stock options. A stock option is an award that entitles the participant to receive stock upon payment of the exercise price. The exercise price of an option may not be less than the fair market value (or, in the case of an ISO granted to a ten percent shareholder, 110% of the fair market value) of a share of our common stock on the date of grant. Our compensation committee will determine the time or times at which stock options become exercisable and the terms on which they remain exercisable.

Stock appreciation rights. A stock appreciation right is an award that entitles the participant to receive stock or cash upon exercise equal to the excess of the value of the shares subject to the right over the base price. The base price of a stock appreciation right may not be less than the fair market value of a share of our common stock on the date of grant. Our compensation committee will determine the time or times at which stock appreciation rights become exercisable and the terms on which they remain exercisable.

Restricted and unrestricted stock. A restricted stock award is an award of common stock subject to forfeiture restrictions, while an unrestricted stock award is not subject to restrictions.

Stock units. A stock unit award is denominated in shares of our common stock and entitles the participant to receive stock or cash measured by the value of the shares in the future. The delivery of stock or cash under a stock unit may be subject to the satisfaction of performance conditions or other vesting conditions.

Performance awards. A performance award is an award the vesting, settlement or exercisability of which is subject to specified performance criteria.

Cash awards: An award that is settled in cash.

Vesting. Our compensation committee has the authority to determine the vesting schedule applicable to each award, and to accelerate the vesting or exercisability of any award.

Termination of Employment. Our compensation committee will determine the effect of termination of employment or service on an award. Unless otherwise provided by our compensation committee or in an award agreement, upon a termination of a participant s employment all unvested options then held by the participant and other awards requiring exercise will terminate and all other unvested awards will be forfeited. Unless otherwise provided for by our compensation committee, all vested stock options and stock appreciation rights then held by the participant will remain outstanding for three months, or one year in the case of death, or, in each case, until the applicable expiration date, if earlier. All stock options and stock appreciation rights held by a participant immediately prior to the participant s termination of employment will immediately terminate upon termination of employment if the termination is for cause as defined in the 2014 Plan or occurs in circumstances that would have constituted grounds for the participant s employment to be terminated for cause, in the determination of the Administrator.

Performance Criteria. The 2014 Plan provides for the grant of performance awards that are made based upon, and subject to achieving, performance objectives. Performance objectives with respect to those awards that are intended to qualify as performance-based compensation for purposes of Section 162(m) of the Code, or Section 162(m) are limited to an objectively determinable measure or measures of performance relating to any or any combination of the following (measured either absolutely or by reference to an index or indices and determined either on a consolidated basis or, as the context permits, on a divisional, subsidiary, line of business, project or geographical basis or in combinations thereof): sales; revenue; assets; expenses; earnings from operations, earnings before or after deduction for all or any portion of interest, taxes, depreciation, amortization, incentives, service fees or extraordinary or special items, whether or not on a continuing operations or an aggregate or per share basis; net income or net income per common share (basic or diluted); return on equity, investment, capital or assets; one or more operating ratios; borrowing levels, leverage ratios or credit rating; market share; capital expenditures; cash flow, free cash flow, cash flow return on investment, or net cash

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provided by operations; stock price, dividends or total stockholder return; development of new technologies or products; sales of particular products or services; economic value created or added; operating margin or profit margin; customer acquisition or retention; raising or refinancing of capital; successful hiring of key individuals; resolution of significant litigation; acquisitions and divestitures (in whole or in part); joint ventures and strategic alliances; spin-offs, split-ups and the like; reorganizations; recapitalizations, restructurings, financings (issuance of debt or equity) or refinancings; or strategic business criteria, consisting of one or more objectives based on the following goals: meeting specified market penetration or value added, product development or introduction (including, without limitation, any clinical trial accomplishments, regulatory or other filings or approvals, or other product development milestones), geographic business expansion, cost targets, cost reductions or savings, customer satisfaction, operating efficiency, acquisition or retention, employee satisfaction, information technology, corporate development (including, without limitation, licenses, innovation, research or establishment of third party collaborations), manufacturing or process development, legal compliance or risk reduction, patent application or issuance goals, or goals relating to acquisitions or divestitures (in whole or in part), joint ventures or strategic alliances.

To the extent consistent with the requirements for satisfying the performance-based compensation exception under Section 162(m), our compensation committee may provide in the case of any award intended to qualify for such exception that one or more of the performance objectives applicable to an award will be adjusted in an objectively determinable manner to reflect events (for example, acquisitions or dispositions) occurring during the performance period of such award that affect the applicable performance objectives.

Transferability. Awards under the 2014 Plan may not be transferred except by will or by the laws of descent and distribution, unless (for awards other than ISOs) otherwise provided by our compensation committee.

Recovery of Compensation; Other Terms. Awards granted under the 2014 Plan are subject to forfeiture, termination and rescission, and a participant will be obligated to return to the company the value received with respect to awards, to the extent provided by our compensation committee in an award agreement, pursuant to Company policy relating to the recovery of erroneously-paid incentive compensation, or as otherwise required by law or applicable stock exchange listing standards.

Covered Transactions. In the event of a consolidation, merger or similar transaction, a sale or transfer of all or substantially all of our assets or our dissolution or liquidation, our compensation committee may, among other things, provide for continuation or assumption of outstanding awards, for new grants in substitution of outstanding awards, for the accelerated vesting or delivery of shares under awards or for a cash-out of outstanding awards, in each case on such terms and with such restrictions as it deems appropriate. Except as our compensation committee may otherwise determine, awards not assumed or continued will automatically terminate and in the case of outstanding shares of restricted stock, will automatically be forfeited upon the consummation of such covered transaction.

Adjustment. In the event of a stock dividend, stock split or combination of shares including a reverse stock split, recapitalization or other change in our capital structure that constitutes an equity restructuring within the meaning of the Financial Accounting Standards Board, Accounting Standards Codification Topic 718, *Compensation Stock Compensation*, our compensation committee will make appropriate adjustments to the maximum number of shares that may be delivered under, and the individual share limits included in, the 2014 Plan, and will also make appropriate adjustments to the number and kind of shares of stock or securities subject to awards, the exercise prices of such awards or any other terms of awards affected by such change. Our compensation committee will also make the types of adjustments described above to take into account distributions and other events other than those listed above if it determines that such adjustments are appropriate to avoid distortion and preserve the value of awards.

Amendment and Termination. Our compensation committee will be able to amend the 2014 Plan or outstanding awards, or terminate the 2014 Plan as to future grants of awards, except that our compensation committee will not be able to alter the terms of an award if it would affect materially and adversely a participant s rights under the award without the participant s consent (unless expressly provided in the 2014 Plan or the right to alter the terms of an award was expressly reserved by our compensation committee at the time the

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award was granted). Stockholder approval will be required for any amendment to the 2014 Plan to the extent such approval is required by law, including the Code or applicable stock exchange requirements.

Employee Stock Purchase Plan

Prior to the completion of this offering, our board of directors intends to adopt the Ultragenyx Pharmaceutical Inc. 2014 Employee Stock Purchase Plan, or the 2014 ESPP, as a means of permitting our eligible employees, including our named executive officers, to acquire shares of our common stock. 600,000 shares of our common stock will be available for issuance under the 2014 ESPP. The number of shares of our common stock available for issuance under the 2014 ESPP will be automatically increased on January 1 of each year, beginning January 1, 2015 through January 1, 2024, by an amount equal to the least of (i) 1,200,000 shares of common stock, (ii) 1% of the number of shares of common stock outstanding on a fully diluted basis as of the close of business on the immediately preceding day (calculated by adding to the number of shares of common stock outstanding, all outstanding securities convertible into common stock on such date on an as converted basis), and (iii) a lesser amount determined by the compensation committee on or prior to January 1 of a given year. Under the 2014 ESPP, eligible employees of the company may purchase shares of our common stock during pre-specified purchase periods at a price equal to the lesser of 85% of the fair market value of a share of our common stock at the beginning of the purchase period or 85% of the fair market value of a share of our common stock at the end of the purchase period. As of the date of this prospectus, our board of directors has not determined the date on which the initial purchase period will commence under the 2014 ESPP, however the initial purchase period will not commence prior to the completion of this offering.

2011 Equity Incentive Plan, as amended

The Ultragenyx Pharmaceutical Inc. 2011 Equity Incentive Plan, which became effective June 14, 2011 and was amended on December 18, 2012 (as so amended, the 2011 Plan), provides for the grant of equity-based awards to participants selected by our board of directors. The following summary of the 2011 Plan is not a complete description of all provisions of the 2011 Plan and is qualified in its entirety by reference to the 2011 Plan, which is filed as an exhibit to the registration statement of which this prospectus is a part. Following this offering, all equity-based awards will be granted under the company s 2014 Plan described above.

Purpose. The purpose of the 2011 Plan is to promote the success and enhance the value of the company by linking the personal interests of the members of the board of directors, employees and consultants of the company and our affiliates to those of the company stockholders and by providing such individuals with an incentive for performance to generate returns to stockholders. The 2011 Plan is also intended to provide the company flexibility in our ability to motivate, attract, and retain the services of such individuals.

Plan Administration. The 2011 Plan is administered by our board of directors, which has authority to determine eligibility for and grant awards and to determine the terms and conditions of all awards, including the time or times upon which awards vest or become exercisable and remain exercisable, and make all other decisions and determinations necessary or advisable to administer the 2011 Plan. The 2011 Plan administrator s determinations under the 2011 Plan are conclusive and binding.

Authorized Shares. Subject to adjustment, the aggregate number of shares of our common stock that may be delivered in satisfaction of awards under the 2011 Plan is 3,756,521 shares. As of September 30, 2013, options to purchase a total of 1,526,772 shares of common stock were issued and outstanding under the 2011 Plan, a total of 664,396 shares of common stock had been issued upon the exercise of options granted under the 2011 Plan and 1,565,352 shares remained available for future grants under the 2011 Plan. Shares of our common stock to be issued under the 2011 Plan may be authorized but unissued shares of our common stock, our treasury stock or, after the completion of this offering, our common stock purchased on the open market. The payment of dividend equivalents in cash will not be counted against the shares available for issuance under the 2011 Plan. Any shares of our common stock underlying awards that expire, terminate, are forfeited or repurchased by us prior to the issuance of stock, or that are withheld in payment of the exercise price of an award or in satisfaction of tax withholding will again be available for issuance under the 2011 Plan.

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Eligibility. The 2011 Plan Administrator selects participants from among our key employees, directors, and consultants and of our affiliates. Eligibility for options intended to be incentive stock options, or ISOs, is limited to employees of the company or certain affiliates.

Types of Awards. The 2011 Plan provides for grants of stock options, restricted stock and stock units, stock appreciation rights and stock payments. Dividend equivalents may also be provided in connection with an award under the 2011 Plan. Under the 2011 Plan only stock options have been granted.

Stock options. A stock option is an award that entitles the participant to receive stock upon payment of the exercise price. The exercise price of an option may not be less than the fair market value (or, in the case of an ISO granted to a ten percent shareholder, 110% of the fair market value) of a share of our common stock on the date of grant. The 2011 Plan administrator determines the time or times at which stock options become exercisable and the terms on which they remain exercisable. The 2011 Plan administrator may permit a participant to exercise an option prior to the full vesting of the award, provided that the shares acquired upon exercise of such option may be subject to forfeiture, transfer or other restrictions imposed by the 2011 Plan administrator.

Restricted stock. A restricted stock award is an award of common stock subject to repurchase, forfeiture and transferability restrictions imposed by the 2011 Plan administrator. Unless the 2011 Plan administrator determines otherwise, upon the termination of a participant s service for any reason, restricted stock shall be forfeited or subject to repurchase by the company.

Transferability. Awards under the 2011 Plan may not be transferred except by will or by the laws of descent and distribution, unless (for awards other than ISOs) the 2011 Plan administrator permits awards to be transferred to, exercised by and paid to a permitted transferee as defined in the 2011 Plan, subject to certain terms and conditions as described in detail in the 2011 Plan.

Corporate Transactions. In the event of any combination or exchange of shares, merger, consolidation, distribution of assets to stockholders (other than normal cash dividends) or similar corporate transaction affecting out stock or the share price of our stock, the 2011 Plan administrator will make proportionate adjustments to the aggregate number and type of shares issuable under the 2011 Plan, the terms and conditions of outstanding, and the grant or exercise price per share of any outstanding awards. In addition, the 2011 Plan administrator may provide for the cash out of existing awards, the assumption or substitution of outstanding awards, an adjustment to the terms and conditions of outstanding awards including the number and type of shares subject to such awards, the acceleration of vesting conditions or the cancellation of outstanding awards.

Change in Control. Unless an award agreement provides otherwise, in the event of a change in control (as defined in the 2011 Plan) if awards are not continued, assumed, or replaced, each award will become fully exercisable and/or payable, as applicable, and all restrictions shall lapse immediately prior to such change in control. Any awards that are continued, assumed, or replaced in connection with the change of control shall become fully exercisable and/or payable, as applicable, and all restrictions shall lapse in the event the participant is terminated in connection with or within 12 months following the change in control, unless such termination is with cause or without good reason, each as defined in the 2011 Plan.

Adjustment. In the event of a stock dividend, stock split, spin-off, rights offering or recapitalization that affects the shares of stock or the share price of stock, the 2011 Plan administrator will make proportionate, nondiscretionary adjustments to the maximum number of shares that may be issued under the 2011 Plan, the number of shares of stock or securities subject to awards, the exercise prices of such awards or any other terms of awards affected by such change.

Amendment and Termination. Our Board may terminate, amend or modify the 2011 Plan; stockholder approval will be required for any amendment to the 2011 Plan to the extent necessary to comply with any applicable law, regulation or stock exchange rule. The 2011 Plan administrator has the authority to cancel any or all outstanding wards under the 2011 Plan with the consent of the affected award holders, and to grant substitute awards. No termination, amendment or modification of the 2011 Plan may adversely affect in any material way any outstanding awards without the prior written consent of the participant. Unless terminated sooner by the 2011

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Plan administrator or extended with stockholder approval, the 2011 Plan will terminate on June 14, 2021. No awards may be granted under our 2011 Plan after it is terminated.

401(k) Plan

We maintain a 401(k) plan for employees. The 401(k) plan is intended to qualify under Section 401(k) of the Code, so that contributions to the 401(k) plan by employees or by us, and the investment earnings thereon, are not taxable to the employees until withdrawn from the 401(k) plan, and so that contributions by us, if any, will be deductible by us when made. Under the 401(k) plan, employees may elect to reduce their current compensation by up to the statutorily prescribed annual limit and to have the amount of such reduction contributed to the 401(k) plan. The 401(k) plan permits us to make contributions up to the limits allowed by law on behalf of all eligible employees. Historically, we have not made any matching contributions to the 401(k) plan.

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CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

The following is a description of transactions since January 1, 2010 to which we have been a party, in which the amount involved exceeds $120,000, and in which any of our directors, executive officers or holders of more than 5% of our capital stock, or an affiliate or immediate family member thereof, had or will have a direct or indirect material interest. We believe the terms obtained or consideration that we paid or received, as applicable, in connection with the transactions described below were comparable to terms available or the amounts that would be paid or received, as applicable, from unaffiliated third parties.

Sales and Purchases of Securities

Series A Convertible Preferred Stock Financing

On June 16, 2011, we sold an aggregate of 18,052,464 shares of our Series A convertible preferred stock to eight investors at a purchase price of $1.034 per share, for an aggregate purchase price of approximately $15.0 million in cash and $3.7 million in converted bridge notes. On July 16, 2012, we sold, pursuant to a second tranche closing, an aggregate of 14,604,895 shares of our Series A convertible preferred stock to six investors at a purchase price of $1.034 per share, for an aggregate purchase price of $15.1 million in cash. The table below sets forth the aggregate number of shares of Series A convertible preferred stock sold to our directors, executive officers or holders of more than 5% of our capital stock, or an immediate family member thereof, as applicable:

Name of Stockholder	Number of Shares of Series A Convertible Preferred Stock	Total Purchase Price
Emil D. Kakkis, M.D., Ph.D.	1,814,944	$ 1,876,471
William Aliski	247,049	$ 255,424

Convertible Notes and Series A Convertible Preferred Stock Warrants

On June 30, 2010, we entered into a Note and Warrant Purchase Agreement with Emil D. Kakkis, M.D., Ph.D. Pursuant to the Note and Warrant Purchase Agreement, we issued a convertible promissory note in the amount of $1.0 million to Dr. Kakkis and also issued him a warrant to purchase up to 241,803 shares of our Series A convertible preferred stock. Emil D. Kakkis, M.D., Ph.D. is our President and Chief Executive Officer and one of our directors.

On February 23, 2011, we entered into a Note and Warrant Purchase Agreement with William Aliski. Pursuant to the Note and Warrant Purchase Agreement, we issued a convertible promissory note in the amount of $250,000 to Mr. Aliski and also issued him a warrant to purchase up to 84,631 shares of our Series A convertible preferred stock. William Aliski is one of our directors.

On June 14, 2011, we entered into a Note and Warrant Purchase Agreement with Emil D. Kakkis, M.D., Ph.D. Pursuant to the Note and Warrant Purchase Agreement, we issued a convertible promissory note in the amount of $300,000 to Dr. Kakkis and also issued him a warrant to purchase up to 72,541 shares of our Series A convertible preferred stock.

On June 14, 2011, we entered into a second Note and Warrant Purchase Agreement with Emil D. Kakkis, M.D., Ph.D. Pursuant to the Note and Warrant Purchase Agreement, we issued a convertible promissory note in the amount of $500,000 to Dr. Kakkis and also issued him a warrant to purchase up to 120,901 shares of our Series A convertible preferred stock.

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Series B Convertible Preferred Stock Financing

On December 18, 2012, we sold an aggregate of 27,081,680 shares of our Series B convertible preferred stock to 34 investors at a purchase price of $2.769 per share, for an aggregate purchase price of approximately $75 million in cash. The table below sets forth the aggregate number of shares of Series B convertible preferred stock sold to our directors, executive officers or holders of more than 5% of our capital stock, or an immediate family member thereof, as applicable:

Name of Stockholder	Number of Shares of Series B Convertible Preferred Stock	Total Purchase Price
TPG Biotechnology Partners III, L.P.	541,634	$ 1,500,001
Beacon Bioventures Fund II Limited Partnership	541,634	$ 1,500,001
HealthCap VI L.P.	481,452	$ 1,333,333
Entities affiliated with A.M. Pappas Life Science Ventures IV, L.P.	240,727	$ 666,669

Indemnification Agreements and Directors and Officers Liability Insurance

We intend to enter into indemnification agreements with each of our executive officers and directors prior to the completion of this offering. We also maintain an insurance policy that covers certain liabilities of directors and officers of our Company arising out of claims based on acts or omissions in their capacities as directors or officers.

Registration Rights Agreement

We and certain holders of our preferred stock have entered into an investor rights agreement pursuant to which these stockholders will have, among other things, registration rights under the Securities Act of 1933, as amended, with respect to common stock that they will hold following this offering. Upon the completion of this offering, all outstanding shares of our preferred stock will be converted into common stock. See Description of Capital Stock Registration Rights for a further description of the terms of these agreements.

Procedures for Related Party Transactions

We have adopted a related person transaction approval policy that will govern the review, approval and/or ratification of related person transactions following the closing of this offering. Pursuant to this policy, if we want to enter into a transaction with a related person or an affiliate or immediate family member of a related person, our chief financial officer will review the proposed transaction to determine, based on applicable NASDAQ and SEC rules, if such transaction qualifies as a related person transaction. If the chief financial officer determines that the proposed transaction is a related person transaction, then the proposed transaction shall be submitted to the audit committee for pre-approval at the next regular or special audit committee meeting; if the chief financial officer, in consultation with the chief executive officer, determines that it is not practicable to wait until the next meeting of the audit committee, then the chief financial officer shall submit the proposed transaction to the chairperson of the audit committee. In the event that our chief executive officer or chief financial officer becomes aware of a related person transaction that has not been previously approved or previously ratified under our related person transaction approval policy, the transaction, if pending or ongoing, will be promptly submitted to the audit committee or the chairperson of the audit committee for consideration. If the transaction is already completed, the audit committee or the chairperson of the audit committee shall evaluate the transaction to determine if rescission of the transaction and/or any disciplinary action is appropriate.

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PRINCIPAL STOCKHOLDERS

The following table sets forth information relating to the beneficial ownership of our common stock as of January 10, 2014, by:

- each person, or group of affiliated persons, known by us to beneficially own more than 5% of our outstanding shares of common stock;
- each of our directors and our nominee for director;
- each of our named executive officers; and
- all directors and executive officers as a group.

The number of shares beneficially owned by each entity, person, director or executive officer is determined in accordance with the rules of the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. Under such rules, beneficial ownership includes any shares over which the individual has sole or shared voting power or investment power as well as any shares that the individual has the right to acquire within 60 days of January 10, 2014 through the exercise of any stock option, warrants or other rights. Except as otherwise indicated, and subject to applicable community property laws, the persons named in the table have sole voting and investment power with respect to all shares of common stock held by that person.

The percentage of shares beneficially owned is computed on the basis of 23,383,381 shares of our common stock outstanding as of January 10, 2014, which reflects the assumed conversion of all of our outstanding shares of preferred stock into an aggregate of 19,598,486 shares of common stock. Shares of our common stock that a person has the right to acquire within 60 days of January 10, 2014 are deemed outstanding for purposes of computing the percentage ownership of the person holding such rights, but are not deemed outstanding for purposes of computing the percentage ownership of any other person, except with respect to the percentage ownership of all directors and executive officers as a group. Unless otherwise indicated below, the address for each beneficial owner listed is c/o Ultragenyx Pharmaceutical Inc., at 60 Leveroni Court, Novato, California 94949.

Name and Address of Beneficial Owner	Number of Shares Beneficially Owned	Percentage of Shares Beneficially Owned: Before Offering	Percentage of Shares Beneficially Owned: After Offering
5% or Greater Stockholders:			
TPG Biotechnology Partners III, L.P.[1]	3,085,240	13.2%	10.6%
Beacon Bioventures Fund II Limited Partnership[2]	3,085,240	13.2%	10.6%
HealthCap VI, L.P.[3]	2,742,436	11.7%	9.4%
Adage Capital Partners, L.P.[4]	1,727,974	7.4%	5.9%
Funds managed by Capital Research Global Investors[5]	1,497,576	6.4%	5.1%
Entities affiliated with A.M. Pappas Life Science Ventures IV, L.P.[6]	1,371,213	5.9%	4.7%
Directors (including our Director Nominees) and Named Executive Officers:			
Eran Nadav, Ph.D.			
Benjamin Auspitz			
Mårten Steen, M.D., Ph.D.			
William Aliski[7]	61,011	*	*
Matthew Fust[8]			
Clay B. Siegall, Ph.D.[8]			
Emil D. Kakkis, M.D., Ph.D.[9]	3,326,181	14.1%	11.4%
Thomas Kassberg[10]	145,406	*	*

Shalini Sharp[11]	83,743	*	*
All executive officers and directors as a group[12] (7 persons)	3,616,341	15.3%	12.3%

* Indicates beneficial ownership of less than 1% of the total outstanding common stock.

(1) Consists of (a) 2,912,443 shares of common stock issuable upon conversion of shares of Series A convertible preferred stock and (b) 172,797 shares of common stock issuable upon conversion of shares of

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Series B convertible preferred stock. TPG Biotechnology Partners III, L.P. is a Delaware limited partnership, whose general partner is TPG Biotechnology GenPar III, L.P., a Delaware limited partnership, whose general partner is TPG Biotechnology GenPar III Advisors, LLC, a Delaware limited liability company, whose sole member is TPG Holdings I, L.P., a Delaware limited partnership, whose general partner is TPG Holdings I-A, LLC, a Delaware limited liability company, whose sole member is TPG Group Holdings (SBS), L.P., a Delaware limited partnership, whose general partner is TPG Group Holdings (SBS) Advisors, Inc., or Group Advisors, a Delaware corporation. Messrs. David Bonderman and James G. Coulter are officers, directors and sole shareholders of Group Advisors and may therefore be deemed to be the beneficial owners of the shares held by TPG Biotechnology Partners III, L.P. The address for Messrs. Bonderman and Coulter is c/o TPG Capital, L.P., 301 Commerce Street, Suite 3300, Fort Worth, TX 76102.

(2) Consists of (a) 2,912,443 shares of common stock issuable upon conversion of shares of Series A convertible preferred stock and (b) 172,797 shares of common stock issuable upon conversion of shares of Series B convertible preferred stock. Beacon Bioventures Advisors Fund II Limited Partnership is the general partner of Beacon Bioventures Fund II Limited Partnership. Beacon Bioventures Advisors Fund II Limited Partnership is solely managed by Northern Neck Investors LLC, its general partner and investment manager. Northern Neck Investors LLC is owned by the shareholders and certain employees of FMR LLC. Northern Neck Investors LLC is managed on a day-to-day basis by its President, Paul L. Mucci, and as such Mr. Mucci may be deemed to share voting and dispositive power with respect to all shares held by Beacon Bioventures Fund II Limited Partnership. Each of the individuals and entities listed above expressly disclaims beneficial ownership of the securities listed above except to the extent of any pecuniary interest therein. The address for each of the individuals and entities listed above is 100 Summer Street R7B, Boston, Massachusetts 02110.

(3) Consists of (a) 2,588,839 shares of common stock issuable upon conversion of shares of Series A convertible preferred stock and (b) 153,597 shares of common stock issuable upon conversion of shares of Series B convertible preferred stock. HealthCap VI GP SA, L.L.C. (HCSA) is the sole general partner of HealthCap VI, L.P. HCSA has voting and dispositive power over the shares held by HealthCap VI, L.P. HCSA disclaims beneficial ownership of such shares, except to the extent of its pecuniary interest therein. Francois Kaiser, Dag Richter, and Daniel Schafer, the members of the board of HCSA, share voting and dispositive power over the shares held by HealthCap VI, L.P. and may be deemed to have indirect beneficial ownership of the shares held by such entities. The members of the board of HCSA disclaim beneficial ownership of shares held by HealthCap VI, L.P. except to the extent of any pecuniary interest therein. The address of HealthCap VI, L.P. is c/o HealthCap VI GP SA, 18, Avenue d Ouchy, 1006 Lausanne, Switzerland.

(4) Consists of 1,727,974 shares of common stock issuable upon conversion of shares of Series B convertible preferred stock. Adage Capital Partners, GP, LLC (ACPGP), serves as the general partner of Adage Capital Partners, L.P., a Delaware limited partnership (the Fund) and as such has discretion over the portfolio of securities beneficially owned by the Fund. Adage Capital Advisors, LLC, a Delaware limited liability company (ACA), is managing member of ACPGP and directs ACPGP s operations. Robert Atchinson and Phillip Gross are the managing members of ACPGP and ACA and general partners of the Fund. Robert Atchinson and Phillip Gross disclaim beneficial ownership of the reported securities except to the extent of their pecuniary interest therein. The address of Adage Capital Partners, L.P. is 200 Clarendon Street, 52nd Floor, Boston, MA 02116.

(5) Consists of (a) 889,970 shares of common stock issuable upon conversion of shares of Series B convertible preferred stock held by SMALLCAP World Fund, Inc. (SCWF) and (b) 607,606 shares of common stock issuable upon conversion of shares of Series B convertible preferred stock held by American Funds Insurance Series Global Small Capitalization Fund (VISC). SCWF and VISC are investment companies registered under the Investment Company Act of 1940, as amended. Capital Research and Management Company (CRMC), an investment adviser registered under the Investment Advisers Act of 1940, as amended, is the investment adviser to SCWF and VISC. CRMC provides investment advisory services to SCWF and VISC through its division Capital Research Global Investors (CRGI). In that capacity, CRGI may be deemed to be the beneficial owner of the shares of Series B convertible preferred

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stock held by SCWF and VISC. CRGI, however, disclaims such beneficial ownership. CRMC has advised that Julian Abdey, Mark E. Denning, Brady L. Enright, J. Blair Frank, Bradford F. Freer, Claudia P. Huntington, Jonathan Knowles, Lawrence Kymisis, Harold H. La, Andraz Razan and Gregory Wendt, as portfolio counselors for SCWF, are primarily responsible for the portfolio management of SCWF, and, as such, have dispositive authority over the shares. CRMC has advised that Mark E. Denning, J. Blair Frank, Claudia P. Huntington, and Harold H. La, as portfolio counselors for VISC, are primarily responsible for the portfolio management of VISC, and, as such, have dispositive authority over the shares. The address for Capital Research and Management Company is 333 S. Hope Street, 55th Floor, Los Angeles, CA 90071.

(6) Consists of (a) 1,235,607 shares of common stock issuable upon conversion of shares of Series A convertible preferred stock held by A.M. Pappas Life Science Ventures IV, L.P., (b) 73,309 shares of common stock issuable upon conversion of shares of Series B convertible preferred stock held by A.M. Pappas Life Science Ventures IV, L.P., (c) 58,808 shares of common stock issuable upon conversion of shares of Series A convertible preferred stock held by PV IV CEO Fund, L.P. and (d) 3,489 shares of common stock issuable upon conversion of shares of Series B convertible preferred stock held by PV IV CEO Fund, L.P. AMP&A Management IV, LLC is the general partner of each of A.M. Pappas Life Science Ventures IV, L.P. and PV IV CEO Fund, L.P. (collectively, the Pappas Funds), and AMP&A Management IV, LLC has a management agreement with A.M. Pappas & Associates, LLC whereby A.M. Pappas & Associates, LLC provides management services for the Pappas Funds. As a result, A.M. Pappas & Associates, LLC s investment committee exercises sole dispositive and voting power over the shares owned by the Pappas Funds. The address for each of A.M. Pappas Life Science Ventures IV, L.P. and PV IV CEO Fund, L.P. is c/o Pappas Ventures, 2520 Meridian Parkway, Suite 400, Durham, NC 27713.

(7) Consists of (a) 31,903 shares of common stock and (b) 29,108 shares of common stock issuable upon conversion of Series A convertible preferred stock that may be acquired pursuant to the exercise of a warrant held by Mr. Aliski.

(8) We expect that this individual will become a member of our board of directors upon the declaration of effectiveness of the registration statement of which this prospectus forms a part.

(9) Consists of (a) 2,552,241 shares of common stock held by the Emil Kakkis and Jenny Soriano Living Trust, dated June 18, 2009, (b) 624,240 shares of common stock issuable upon conversion of shares of Series A convertible preferred stock held by Dr. Kakkis and (c) 149,700 shares of common stock issuable upon conversion of Series A convertible preferred stock that may be acquired pursuant to the exercise of a warrant held by Dr. Kakkis. Dr. Kakkis shares voting and dispositive power over the 2,552,241 shares of common stock held by the Emil Kakkis and Jenny Soriano Living Trust, dated June 18, 2009; each of Dr. Kakkis and Ms. Soriano is a trustee of such trust. Dr. Kakkis has sole voting and dispositive power over the 624,240 shares of common stock issuable upon conversion of shares of Series A convertible preferred stock and the 149,700 shares of common stock issuable upon conversion of Series A convertible preferred stock that may be acquired pursuant to the exercise of a warrant held by Dr. Kakkis.

(10) Consists of (a) 92,850 shares of common stock, (b) 31,454 shares of common stock issuable upon conversion of Series A convertible preferred stock and (c) 21,102 shares of common stock issuable upon the exercise of stock options within 60 days of January 10, 2014.

(11) Consists of (a) 63,804 shares of common stock and (b) 19,939 shares of common stock issuable upon the exercise of stock options within 60 days of January 10, 2014.

(12) Consists of (a) 3,396,492 shares held by our directors and officers and entities affiliated with certain of our directors, (b) 178,808 shares of common stock issuable upon the conversion of shares of preferred stock that may be acquired pursuant to the exercise of warrants by our certain of our directors and officers, and (c) 41,041 shares of common stock issuable upon the exercise of stock options within 60 days of January 10, 2014 held by our officers.

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DESCRIPTION OF CAPITAL STOCK

The following summary describes our capital stock and the material provisions of our amended and restated certificate of incorporation and our amended and restated bylaws, which will become effective in connection with the completion of this offering, warrants to purchase shares of our Series A convertible preferred stock, the amended and restated investor rights agreement to which we and certain of our stockholders are parties, and of the Delaware General Corporation Law. Because the following is only a summary, it does not contain all of the information that may be important to you. For a complete description, you should refer to our amended and restated certificate of incorporation, amended and restated bylaws, warrants to purchase shares of our Series A convertible preferred stock, and amended and restated investor rights agreement, copies of which have been filed as exhibits to the registration statement of which this prospectus is part.

General

Upon completion of this offering, our authorized capital stock will consist of 250,000,000 shares of common stock, par value $0.001 per share, and 25,000,000 shares of preferred stock, par value $0.001 per share. The following description of our capital stock is intended as a summary only and is qualified in its entirety by reference to our amended and restated certificate of incorporation, and amended and restated bylaws, each to be in effect in connection with the closing of this offering, which are filed as exhibits to the registration statement, of which this prospectus forms a part, and to the applicable provisions of the Delaware General Corporation Law.

Common Stock

As of September 30, 2013, there were 23,301,502 shares of our common stock outstanding, held of record by 56 stockholders, which assumes the conversion of all outstanding shares of preferred stock for shares of our common stock. Based on shares outstanding as of September 30, 2013, upon completion of this offering, there will be 29,061,871 shares of our common stock outstanding.

Holders of our common stock are entitled to one vote for each share of common stock held of record for the election of directors and on all matters submitted to a vote of stockholders. Holders of our common stock are entitled to receive dividends ratably, if any, as may be declared by our board of directors out of legally available funds, subject to any preferential dividend rights of any preferred stock then outstanding. Upon our dissolution, liquidation or winding up, holders of our common stock are entitled to share ratably in our net assets legally available after the payment of all our debts and other liabilities, subject to the preferential rights of any preferred stock then outstanding. Holders of our common stock have no preemptive, subscription, redemption or conversion rights. The rights, preferences and privileges of holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future. Except as described below in Anti-Takeover Effects of Delaware Law, Our Certificate of Incorporation and Our By-laws, the affirmative vote of a majority of our outstanding shares of capital stock is generally required to take action under our Certificate of Incorporation and By-laws.

Preferred Stock

Upon completion of this offering, our board of directors will be authorized, without action by the stockholders, to designate and issue up to an aggregate of 25,000,000 shares of preferred stock in one or more series. The board of directors can fix the rights, preferences and privileges of the shares of each series and any of its qualifications, limitations or restrictions. Our board of directors may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of common stock. The issuance of preferred stock, while providing flexibility in connection with possible future financings and acquisitions and other corporate purposes could, under certain circumstances, have the effect of delaying or preventing a change in control of our company and might harm the market price of our common stock.

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Our board of directors will make any determination to issue such shares based on its judgment as to our best interests and the best interests of our stockholders. We have no current plans to issue any shares of preferred stock.

Certain of our stockholders hold, as of the date of this prospectus, 34,349,894 shares of our Series A convertible preferred stock and 27,081,680 shares of our Series B convertible preferred stock. As a result of the reverse stock split we effected on January 17, 2014, each share of Series A and Series B convertible preferred stock outstanding will be converted into shares of our common stock on a 3.1345-for-1 basis. Holders of substantially all of the shares of our preferred stock are subject to lock-up agreements with the underwriters that restrict the sale of our securities for 180 days following the date of this prospectus. See Underwriting for a description of these lock-up agreements.

Warrants

As of September 30, 2013, warrants to purchase a total of 1,027,662 shares of our Series A convertible preferred stock were outstanding with an exercise price of $1.034 per share. These warrants to purchase 1,027,662 shares of Series A convertible preferred stock, which will be converted into warrants to purchase 353,459 shares of common stock with an exercise price of $3.006 per share upon completion of this offering, are exercisable immediately and each expire on the first to occur of (i) the closing date of any reorganization, consolidation or merger of the Company, transfer of all or substantially all of the assets of the Company or any simultaneous sale of more than a majority of the then outstanding securities of the Company other than a mere reincorporation transaction, or (ii) the 10 year anniversary of the date of such warrant which in the case of the outstanding warrants of the Company is June 2020, February 2021 and June 2021, respectively.

Registration Rights

We are party to an amended and restated investors rights agreement, dated as of December 18, 2012, with the holders of shares of our common stock issuable upon conversion of the shares of preferred stock. Following this offering, the holders of approximately 19.6 million shares, or 20.0 million including the shares underlying outstanding warrants, will have the right to require us to register their shares under the Securities Act of 1933, as amended. These shares will represent approximately 69% of our outstanding common stock after this offering, or approximately 67% if the underwriters exercise their option to purchase additional shares in full. These shares also may be sold under Rule 144 under the Securities Act of 1933, depending on their holding period and subject to restrictions in the case of shares held by persons deemed to be our affiliates. The registration rights will terminate upon the later of (i) the fifth anniversary of the closing date of this offering and (ii) as to any holder of registrable securities, such earlier time after this offering at which such holder holds 1% or less of our common stock and all registrable securities held by such holder can be sold in any 90-day period without registration in compliance with Rule 144.

Demand Registration Rights

Under the amended and restated investors rights agreement, beginning 180 days following the effectiveness of the registration statement of which this prospectus forms a part or 45 days following the effective date of any other Company-initiated registration statement, the holders of at least 50% of the registrable shares (or a lesser percentage if the anticipated aggregate offering price is not less than $10 million) then outstanding can, on not more than two occasions, demand that we file a registration statement or request that their shares be included on a registration statement that we are otherwise filing, in either case, registering the resale of their shares of common stock. We are required to use our best efforts to effect the registration and will pay all registration expenses, other than underwriting discounts and commissions, related to any demand registration. These registration rights are subject to conditions and limitations, including the right, in certain circumstances, of the underwriters of an offering to limit the number of shares included in such registration and our right, in certain circumstances, not to effect a requested registration.

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Piggyback Registration Rights

If we propose to register any of our securities under the Securities Act for our own account or the account of any other holder, the significant holders (as defined in the amended and restated investors rights agreement) are entitled to notice of such registration and to request that we include registrable shares for resale on such registration statement, subject to the right of any underwriter to limit the number of shares included in such registration.

We will pay all registration expenses, other than underwriting discounts and commissions, related to any piggyback registration. The amended and restated investors rights agreement contains customary cross-indemnification provisions, pursuant to which we are obligated to indemnify the selling stockholders, in the event of misstatements or omissions in the registration statement attributable to us and they are obligated to indemnify us for misstatements or omissions attributable to them.

Form S-3 Registration Rights

The holders of at least 10% of the registrable securities outstanding can make a written request that we register their shares on Form S-3 if we are eligible to file a registration statement on Form S-3 and if the aggregate price to the public of the shares offered is at least $1 million. These stockholders may make an unlimited number of requests for registration on Form S-3. However, we will not be required to effect a registration on Form S-3 if we determine that such a registration would be seriously detrimental to us and our stockholders or if we have already effected three registration statements on Form S-3 in the 12-month period preceding the date of the request. We will pay all registration expenses, other than underwriting discounts and commissions, related to any S-3 registration.

Voting Agreement, Right of First Refusal and Co-Sale Agreement and Market Stand-Off Provision

We are party to an amended and restated voting agreement and an amended and restated right of first refusal and co-sale agreement, each dated as of December 18, 2012, with all holders of our preferred stock and certain holders of our common stock. These agreements provide for certain rights and obligations, such as rights to designate and covenants with regard to voting for board members and stock transfer restrictions. These agreements will terminate upon the completion of this offering. The market stand-off provision under our amended and restated investors rights agreement shall survive the completion of this offering. See Shares Eligible for Future Sales Lock-Up Agreements.

Anti-Takeover Effects of Delaware Law, our Certificate of Incorporation and Our By-laws

Our certificate of incorporation and by-laws include a number of provisions that may have the effect of encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions include the items described below.

Board Composition and Filling Vacancies

In accordance with our certificate of incorporation, our board is divided into three classes serving three-year terms, with one class being elected each year. Our certificate of incorporation also provides that directors may be removed only for cause. Furthermore, any vacancy on our board of directors, however occurring, including a vacancy resulting from an increase in the size of our board, may only be filled by a resolution of the board.

No Written Consent of Stockholders

Our certificate of incorporation provides that all stockholder actions are required to be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting.

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Meetings of Stockholders

Our certificate of incorporation and by-laws provide that, subject to any rights of holders of any series of preferred stock, only the board or the chairman of the board may call special meetings of stockholders and only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders. Our by-laws limit the business that may be conducted at an annual meeting of stockholders to those matters properly brought before the meeting.

Advance Notice Requirements

Our by-laws establish advance notice procedures with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders. These procedures provide that notice of stockholder proposals must be timely given in writing to our corporate secretary prior to the meeting at which the action is to be taken. Generally, to be timely, notice must be received at our principal executive offices not less than 90 days or more than 120 days prior to the first anniversary date of the annual meeting for the preceding year. The notice must contain certain information specified in the by-laws. These provisions may have the effect of precluding the conduct of certain business at a meeting if the proper procedures are not followed. These provisions may also discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer s own slate of directors or otherwise attempting to obtain control of our company.

Amendment to By-laws and Certificate of Incorporation

As required by the Delaware General Corporation Law, any amendment of our certificate of incorporation must first be approved by a majority of our board of directors and, if required by law or our certificate of incorporation, thereafter be approved by a majority of the outstanding shares entitled to vote on the amendment, and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of the provisions relating to directors, stockholders, the amendment of our by-laws and certificate of incorporation and exclusive jurisdiction of Delaware Courts must be approved by not less than 75% of the outstanding shares entitled to vote on the amendment, and not less than 75% of the outstanding shares of each class entitled to vote thereon as a class. Our by-laws may be amended by the affirmative vote of a majority of the directors then in office, subject to any limitations set forth in the by-laws, and may also be amended by the affirmative vote of at least 75% of the outstanding shares entitled to vote on the amendment.

Blank Check Preferred Stock

Our certificate of incorporation provides for 25,000,000 authorized shares of preferred stock. The existence of authorized but unissued shares of preferred stock may enable our board of directors to render more difficult or to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in the best interests of us or our stockholders, our board of directors could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer or insurgent stockholder or stockholder group. In this regard, our certificate of incorporation grants our board of directors broad power to establish the rights and preferences of authorized and unissued shares of preferred stock. The issuance of shares of preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

Section 203 of the Delaware General Corporation Law

Upon completion of this offering, we will be subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly-held Delaware corporation from engaging

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in a business combination with an interested stockholder for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. A business combination includes, among other things, a merger, asset or stock sale or other transaction resulting in a financial benefit to the interested stockholder. An interested stockholder is a person who, together with affiliates and associates, owns, or did own within three years prior to the determination of interested stockholder status, 15% or more of the corporation s voting stock.

Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- before the stockholder became interested, the board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances; or
- at or after the time the stockholder became interested, the business combination was approved by the board of directors of the corporation and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

A Delaware corporation may opt out of these provisions with an express provision in its original certificate of incorporation or an express provision in its certificate of incorporation or by-laws resulting from a stockholders amendment approved by at least a majority of the outstanding voting shares. We have not opted out of these provisions. As a result, mergers or other takeover or change in control attempts of us may be discouraged or prevented.

Exclusive Jurisdiction of Certain Actions

Our certificate of incorporation requires, to the fullest extent permitted by law, that derivative actions brought in our name, actions against our directors, officers and employees for breach of fiduciary duty and other similar actions may be brought only in the Court of Chancery in the State of Delaware, unless we otherwise consent. Although we believe this provision benefits us by providing increased consistency in the application of Delaware law in the types of lawsuits to which it applies, the provision may have the effect of discouraging lawsuits against our directors and officers. Although our certificate of incorporation contains the choice of forum provision described above, it is possible that a court could rule that such a provision is inapplicable for a particular claim or action or that such provision is unenforceable.

NASDAQ Global Select Market listing

Our common stock has been approved for listing on The NASDAQ Global Select Market under the symbol RARE .

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC. The transfer agent and registrar s address is 620 15th Avenue, Brooklyn, New York 11219.

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SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, there has been no public market for our common stock. Future sales of our common stock, including shares issued upon the exercise of outstanding options or warrants, in the public market after this offering, or the perception that those sales may occur, could cause the prevailing market price for our common stock to fall or impair our ability to raise equity capital in the future. As described below, only a limited number of shares of our common stock will be available for sale in the public market for a period of several months after completion of this offering due to contractual and legal restrictions on resale described below. Future sales of our common stock in the public market either before (to the extent permitted) or after restrictions lapse, or the perception that those sales may occur, could adversely affect the prevailing market price of our common stock at such time and our ability to raise equity capital at a time and price we deem appropriate.

Sale of Restricted Shares

As of September 30, 2013, based on the number of shares of our common stock then outstanding and an initial public offering price of $21.00 per share, upon the closing of this offering, and assuming (1) the conversion of our outstanding preferred stock into shares of our common stock, (2) no exercise of the underwriters option to purchase additional shares of common stock and (3) no exercise of outstanding options or warrants, we would have had outstanding an aggregate of approximately 29,061,871 shares of common stock. Of these shares, all of the 5,760,369 shares of common stock to be sold in this offering, and any shares sold upon exercise of the underwriters option to purchase additional shares, other than the shares purchased by our directors and officers in the directed share program, will be freely tradable in the public market without restriction or further registration under the Securities Act of 1933, as amended, or the Securities Act, unless the shares are held by any of our affiliates as such term is defined in Rule 144 of the Securities Act. All remaining shares of common stock held by existing stockholders immediately prior to the completion of this offering will be restricted securities as such term is defined in Rule 144. These restricted securities were issued and sold by us in private transactions and are eligible for public sale only if registered under the Securities Act or if they qualify for an exemption from registration under the Securities Act, including the exemptions provided by Rule 144 or Rule 701, which rules are summarized below.

As a result of the lock-up agreements referred to below and the provisions of Rule 144 and Rule 701 under the Securities Act, the shares of our common stock (excluding the shares sold in this offering) that will be available for sale in the public market are as follows:

Approximate Number of Shares	First Date Available for Sale into Public Market
23,208,750	180 days after the date of this prospectus upon expiration of the lock-up agreements referred to below, subject in some cases to applicable volume limitations under Rule 144

Lock-Up Agreements and Market Stand-Off Provision

In connection with this offering, we, our directors, our executive officers, substantially all of our stockholders, and substantially all of our option holders who are not also stockholders have agreed, subject to certain exceptions, with the underwriters not to dispose of or hedge any shares of our common stock or securities convertible into or exchangeable for shares of common stock during the period from the date of the lock-up agreement continuing through the date 180 days after the date of this prospectus, except with the prior written consent of J.P. Morgan Securities LLC and Morgan Stanley & Co. LLC, together the representatives of the underwriters. The representatives of the underwriters have advised us that they have no current intent or arrangement to release any of the shares subject to the lock-up agreements prior to the expiration of the lock-up period.

Following the lock-up periods set forth in the agreements described above, and assuming that the representatives of the underwriters do not release any parties from these agreements, all of the shares of our common stock that are restricted securities or are held by our affiliates as of the date of this prospectus will be eligible for sale in the public market in compliance with Rule 144 under the Securities Act.

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In addition, pursuant to our amended and restated investors rights agreement, the parties thereto have agreed under a market stand-off provision that, subject to certain conditions, they will not, directly or indirectly, without the prior written consent of the Company and the managing underwriter, during the same 180-day restricted period referred to above, (i) lend, offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, any shares of our common stock or any securities convertible into or exercisable or exchangeable for common stock or (ii) enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of common stock.

As of the date of this prospectus, holders of approximately 23.2 million shares of common stock (including shares of our preferred stock that will be converted into shares of our common stock upon completion of this offering), or 99.6% of our outstanding shares of common stock on an as-converted basis, are, collectively subject to lock-up restrictions as parties to these agreements or lock-up agreements with the underwriters.

Rule 144

In general, under Rule 144, as currently in effect, once we have been subject to the public company reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act, for at least 90 days, a person (or persons whose shares are required to be aggregated) who is not deemed to have been one of our affiliates for purposes of Rule 144 at any time during the three months preceding a sale, and who has beneficially owned restricted securities within the meaning of Rule 144 for at least six months, including the holding period of any prior owner other than one of our affiliates, is entitled to sell those shares in the public market (subject to the lock-up agreement referred to above, if applicable) without complying with the manner of sale, volume limitations or notice provisions of Rule 144, but subject to compliance with the public information requirements of Rule 144. If such a person has beneficially owned the shares proposed to be sold for at least one year, including the holding period of any prior owner other than affiliates, then such person is entitled to sell such shares in the public market without complying with any of the requirements of Rule 144 (subject to the lock-up agreement referred to above, if applicable).

In general, under Rule 144, as currently in effect, once we have been subject to the public company reporting requirements of the Exchange Act for at least 90 days, our affiliates, as defined in Rule 144, who have beneficially owned the shares proposed to be sold for at least six months are entitled to sell in the public market, upon expiration of any applicable lock-up agreements and within any three-month period, a number of those shares of our common stock that does not exceed the greater of:

- one percent of the number of common shares then outstanding, which will equal approximately 290,618 shares of common stock immediately after this offering (calculated on the basis of the number of shares of our common stock outstanding as of September 30, 2013, the assumptions described above and assuming no exercise of the underwriter s option to purchase additional shares and no exercise of outstanding options or warrants); or

- the average weekly trading volume of our common stock on The NASDAQ Global Select Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to such sale.

Such sales under Rule 144 by our affiliates or persons selling shares on behalf of our affiliates are also subject to certain manner of sale provisions, notice requirements and to the availability of current public information about us.

Notwithstanding the availability of Rule 144, the holders of substantially all of our restricted securities have entered into lock-up agreements as referenced above and their restricted securities will become eligible for sale (subject to the above limitations under Rule 144) upon the expiration of the restrictions set forth in those agreements.

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Rule 701

In general, under Rule 701 as currently in effect, any of our employees, directors, officers, consultants or advisors who acquired common stock from us in connection with a written compensatory stock or option plan or other written agreement in compliance with Rule 701 under the Securities Act before the effective date of the registration statement of which this prospectus is a part (to the extent such common stock is not subject to a lock-up agreement) is entitled to rely on Rule 701 to resell such shares beginning 90 days after we become subject to the public company reporting requirements of the Exchange Act in reliance on Rule 144, but without compliance with the holding period requirements contained in Rule 144. Accordingly, subject to any applicable lock-up agreements, beginning 90 days after we become subject to the public company reporting requirements of the Exchange Act, under Rule 701 persons who are not our affiliates, as defined in Rule 144, may resell those shares without complying with the minimum holding period or public information requirements of Rule 144, and persons who are our affiliates may resell those shares without compliance with Rule 144 s minimum holding period requirements (subject to the terms of the lock-up agreement referred to below, if applicable).

Equity Incentive Plans and Employee Stock Purchase Plan

We intend to file with the SEC a registration statement under the Securities Act covering the shares of common stock that we may issue (i) upon exercise of outstanding options under the 2011 Equity Incentive Plan and reserved for issuance under the 2014 Incentive Plan, and (ii) pursuant to the 2014 Employee Stock Purchase Plan. Such registration statement is expected to be filed and become effective as soon as practicable after the completion of this offering. Accordingly, shares registered under such registration statement will be available for sale in the open market following its effective date, subject to Rule 144 volume limitations and the lock-up agreements described above, if applicable.

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MATERIAL U.S. FEDERAL INCOME TAX CONSEQUENCES TO NON-U.S. HOLDERS

The following discussion is a summary of the material U.S. federal income tax consequences to non-U.S. holders (as defined below) of the purchase, ownership and disposition of our common stock issued pursuant to this offering, but does not purport to be a complete analysis of all potential tax effects. The effects of other U.S. federal tax laws, such as estate and gift tax laws, and any applicable state, local or foreign tax laws are not discussed. This discussion is based on the Internal Revenue Code of 1986, as amended, or the Code, Treasury Regulations promulgated under the Code, judicial decisions, and published rulings and administrative pronouncements of the U.S. Internal Revenue Service, or IRS, in effect as of the date of this offering. These authorities may change or be subject to differing interpretations. Any such change may be applied retroactively in a manner that could adversely affect a non-U.S. holder of our common stock. We have not sought and will not seek any rulings from the IRS regarding the matters discussed below. There can be no assurance the IRS or a court will not take a contrary position regarding the tax consequences of the purchase, ownership and disposition of our common stock.

This discussion is limited to non-U.S. holders that hold our common stock as a capital asset within the meaning of Section 1221 of the Code (property held for investment). This discussion does not address all U.S. federal income tax consequences relevant to a non-U.S. holder s particular circumstances. In addition, it does not address consequences relevant to non-U.S. holders subject to particular rules, including, without limitation:

- U.S. expatriates and certain former citizens or long-term residents of the United States;
- persons subject to the alternative minimum tax;
- persons holding our common stock as part of a hedge, straddle or other risk reduction strategy or as part of a conversion transaction or other integrated investment;
- banks, insurance companies and other financial institutions;
- real estate investment trusts or regulated investment companies;
- brokers, dealers or traders in securities;
- controlled foreign corporations, passive foreign investment companies and corporations that accumulate earnings to avoid U.S. federal income tax;
- S corporations, partnerships or other entities or arrangements treated as partnerships for U.S. federal income tax purposes;
- tax-exempt organizations or governmental organizations;
- persons deemed to sell our common stock under the constructive sale provisions of the Code;
- persons who hold or receive our common stock pursuant to the exercise of any employee stock option or otherwise as compensation; and

tax-qualified retirement plans.

If a partnership (or other entity treated as a partnership for U.S. federal income tax purposes) holds our common stock, the tax treatment of a partner in the partnership will depend on the status of the partner, the activities of the partnership and certain determinations made at the partner level. Accordingly, partnerships holding our common stock and the partners in such partnerships should consult their tax advisors regarding the U.S. federal income tax consequences to them.

THIS DISCUSSION IS FOR INFORMATION PURPOSES ONLY AND IS NOT INTENDED AS TAX ADVICE. INVESTORS SHOULD CONSULT THEIR TAX ADVISORS WITH RESPECT TO THE APPLICATION OF THE U.S. FEDERAL INCOME TAX LAWS TO THEIR PARTICULAR SITUATIONS AS WELL AS ANY TAX CONSEQUENCES OF THE PURCHASE, OWNERSHIP AND DISPOSITION OF OUR COMMON STOCK ARISING UNDER THE U.S. FEDERAL ESTATE OR GIFT TAX LAWS OR UNDER THE LAWS OF ANY STATE, LOCAL OR NON-U.S. TAXING JURISDICTION OR UNDER ANY APPLICABLE INCOME TAX TREATY.

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Definition of a Non-U.S. Holder

For purposes of this discussion, a non-U.S. holder is any beneficial owner of our common stock that is neither a U.S. person nor a partnership for United States federal income tax purposes. A U.S. person is any of the following:

- an individual who is a citizen or resident of the United States;
- a corporation (or other entity taxable as a corporation for U.S. federal income tax purposes) created or organized under the laws of the United States, any state thereof, or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income tax regardless of its source; or
- a trust that (1) is subject to the primary supervision of a U.S. court and the control of one or more United States persons (within the meaning of Section 7701(a)(30) of the Code), or (2) has a valid election in effect to be treated as a United States person for U.S. federal income tax purposes.

Distributions

As described in the section entitled Dividend Policy, we do not anticipate declaring or paying dividends to holders of our common stock in the foreseeable future. However, if we do make distributions on our common stock, such distributions of cash or property on our common stock will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. Amounts not treated as dividends for U.S. federal income tax purposes will constitute a return of capital and first be applied against and reduce a non-U.S. holder s adjusted tax basis in its common stock, but not below zero. Any excess will be treated as capital gain and will be treated as described below in the section titled Sale or Other Taxable Disposition.

Dividends paid to a non-U.S. holder of our common stock generally will be subject to U.S. federal withholding tax at a rate of 30% of the gross amount of the dividends (or such lower rate specified by an applicable income tax treaty). Even if a non-U.S. holder is eligible for a lower treaty rate, dividend payments will generally be subject to withholding at a 30% rate (rather than the lower treaty rate) unless the non-U.S. holder provides a valid IRS Form W-8BEN (or applicable successor form) certifying such holder s qualification for the reduced rate.

Non-U.S. holders who do not timely provide us or our paying agent with the required certification, but who qualify for a reduced treaty rate, may obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS. Non-U.S. holders should consult their tax advisors regarding their entitlement to benefits under a tax treaty.

Subject to the discussions below regarding backup withholding and foreign accounts, if dividends paid to a non-U.S. holder are effectively connected with the non-U.S. holder s conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, the non-U.S. holder maintains a permanent establishment in the United States to which such dividends are attributable), the non-U.S. holder will be exempt from U.S. federal withholding tax. To claim the exemption, the non-U.S. holder must furnish to us or our paying agent a valid IRS Form W-8ECI (or applicable successor form), certifying that the dividends are effectively connected with the non-U.S. holder s conduct of a trade or business within the United States.

Any dividends paid on our common stock that are effectively connected with a non-U.S. holder s U.S. trade or business (and, if required by an applicable tax treaty, attributable to a permanent establishment maintained by the non-U.S. holder in the United States) generally will be subject to U.S. federal income tax on a net income basis in the same manner as if such holder were a U.S. person. A non-U.S. holder that is a corporation also may be subject to a branch profits tax at a rate of 30% (or such lower rate specified by an applicable tax treaty) of a portion of its effectively connected earnings and profits for the taxable year. Non-U.S. holders should consult their tax advisors regarding any applicable tax treaties that may provide for different rules.

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Sale or Other Taxable Disposition

Subject to the discussions below regarding backup withholding and foreign accounts, a non-U.S. holder will not be subject to U.S. federal income tax on any gain realized upon the sale or other disposition of our common stock unless:

- the gain is effectively connected with the non-U.S. holder s conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, the non-U.S. holder maintains a permanent establishment in the United States to which such gain is attributable);
- the non-U.S. holder is a nonresident alien individual present in the United States for 183 days or more during the taxable year of the disposition and certain other requirements are met; or
- our common stock constitutes a U.S. real property interest, or USRPI, by reason of our status as a U.S. real property holding corporation, or a USRPHC, for U.S. federal income tax purposes.

Gain described in the first bullet point above will generally be subject to U.S. federal income tax on a net income basis at the regular graduated U.S. federal income tax rates. A non-U.S. holder that is a foreign corporation also may be subject to a branch profits tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on such effectively connected gain, as adjusted for certain items.

A non-U.S. holder described in the second bullet point above will be subject to U.S. federal income tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on any gain derived from the disposition, which may be offset by certain U.S. source capital losses of the non-U.S. holder (even though the individual is not considered a resident of the United States) provided the non-U.S. holder has timely filed U.S. federal income tax returns with respect to such losses.

With respect to the third bullet point above, we believe we are not currently and do not anticipate becoming a USRPHC. However, because the determination of whether we are a USRPHC depends on the fair market value of our USRPIs relative to the fair market value of our other business assets and our non-U.S. real property interests, there can be no assurance we are not a USRPHC or will not become one in the future. Even if we are or were to become a USRPHC, gain arising from the sale or other taxable disposition by a non-U.S. holder of our common stock will not be subject to U.S. federal income tax if our common stock is regularly traded, as defined by applicable Treasury Regulations, on an established securities market, and such non-U.S. holder owned, actually or constructively, 5% or less of our common stock throughout the shorter of the five-year period ending on the date of the sale or other disposition or the non-U.S. holder s holding period.

Non-U.S. holders should consult their tax advisors regarding potentially applicable income tax treaties that may provide for different rules.

Information Reporting and Backup Withholding

A non-U.S. holder will not be subject to backup withholding with respect to payments of dividends on our common stock we make to the non-U.S. holder, provided the holder certifies its non-U.S. status, such as by providing a valid IRS Form W-8BEN or W-8ECI, or otherwise establishes an exemption. However, information returns will be filed with the IRS in connection with any dividends on our common stock paid to the non-U.S. holder, regardless of whether any tax was actually withheld. Copies of these information returns may also be made available under the provisions of a specific treaty or agreement to the tax authorities of the country in which the non-U.S. holder resides or is established.

Information reporting and, depending on the circumstances, backup withholding will apply to the proceeds of a sale of our common stock within the United States or conducted through certain U.S.-related financial intermediaries, unless the beneficial owner certifies under penalty of perjury that it is a non-U.S. holder on Form W-8BEN or other applicable form or such owner otherwise establishes an exemption.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules may be allowed as a refund or a credit against a non-U.S. holder s U.S. federal income tax liability, provided the required information is timely furnished to the IRS.

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Additional Withholding Tax on Payments Made to Foreign Accounts

Legislation incorporating provisions referred to as the Foreign Account Tax Compliance Act, or FATCA, was enacted March 18, 2010. A 30% withholding tax may be imposed on dividends paid on, and the gross proceeds from the sale or other disposition of, our common stock paid to a foreign financial institution (as defined in the Code) or to a non-financial foreign entity (as defined in the Code) (whether such foreign financial institution or non-financial foreign entity is the beneficial owner or an intermediary), unless (1) the foreign financial institution undertakes certain diligence and reporting obligations, (2) the non-financial foreign entity either certifies it does not have any substantial United States owners (as defined in the Code) or furnishes identifying information regarding each substantial United States owner, or (3) the foreign financial institution or non-financial foreign entity otherwise qualifies for an exemption from these rules. If the payee is a foreign financial institution and is subject to the diligence and reporting requirements in (1) above, it must enter into an agreement with the U.S. Department of the Treasury requiring, among other things, that it undertake to identify accounts held by certain U.S. persons or U.S.-owned foreign entities (as defined in applicable Treasury Regulations), annually report certain information about such accounts, and withhold 30% on payments to non-compliant foreign financial institutions and certain other account holders. Foreign governments may enter into an agreement with the IRS to implement FATCA in a different manner. Under current IRS guidance, FATCA withholding will apply to payments of dividends on our common stock made on or after July 1, 2014, and to payments of gross proceeds from the sale or other disposition of such stock on or after January 1, 2017. Prospective investors should consult their tax advisors regarding these withholding provisions.

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UNDERWRITING

We are offering the shares of common stock described in this prospectus through a number of underwriters. J.P. Morgan Securities LLC and Morgan Stanley & Co. LLC are acting as joint book-running managers of the offering and as representatives of the underwriters. We have entered into an underwriting agreement with the underwriters. Subject to the terms and conditions of the underwriting agreement, we have agreed to sell to the underwriters, and each underwriter has severally agreed to purchase, at the public offering price less the underwriting discounts and commissions set forth on the cover of this prospectus, the number of shares of common stock listed next to its name in the following table:

Name	Number of shares
J.P. Morgan Securities LLC	2,304,148
Morgan Stanley & Co. LLC	1,958,526
Cowen and Company, LLC	1,209,677
Canaccord Genuity Inc.	288,018
Total	5,760,369

The underwriters are committed to purchase all the shares of common stock offered by us if they purchase any shares. The underwriting agreement also provides that if an underwriter defaults, the purchase commitments of non-defaulting underwriters may also be increased or the offering may be terminated.

The underwriters propose to offer the shares of common stock directly to the public at the initial public offering price set forth on the cover of this prospectus and to certain dealers at that price less a concession not in excess of $0.882 per share. Any such dealers may resell shares to certain other brokers or dealers at a discount of up to $0.882 per share from the initial public offering price. After the initial public offering of the shares, the offering price and other selling terms may be changed by the underwriters. Sales of shares made outside of the United States may be made by affiliates of the underwriters.

The underwriters have an option to buy up to 864,054 additional shares of common stock from us to cover sales of shares by the underwriters which exceed the number of shares specified in the table above. The underwriters have 30 days from the date of this prospectus to exercise this option to purchase additional shares. If any shares are purchased with this option to purchase additional shares, the underwriters will purchase shares in approximately the same proportion as shown in the table above.

The underwriting fee is equal to the public offering price per share of common stock less the amount paid by the underwriters to us per share of common stock. The underwriting fee is $1.47 per share. The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters assuming both no exercise and full exercise of the underwriters option to purchase additional shares.

	Without exercise of option to purchase additional shares	With full exercise of option to purchase additional shares
Per share	$ 1.47	$ 1.47
Total	$ 8,467,742	$ 9,737,902

We estimate that the total expenses of this offering, including registration, filing and listing fees, printing fees and legal and accounting expenses, but excluding the underwriting discounts and commissions, will be approximately $3.0 million. We have agreed to reimburse the underwriters for all expenses relating to the clearance of this offering with the Financial Industry Regulatory Authority (in an amount not to exceed $25,000).

A prospectus in electronic format may be made available on the web sites maintained by one or more underwriters, or selling group members, if any, participating in the offering. The underwriters may agree to allocate a number of shares to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the representatives to underwriters and selling group members that may make Internet distributions on the same basis as other allocations.

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We have agreed that we will not (i) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, or file with the Securities and Exchange Commission a registration statement under the Securities Act of 1933, as amended (the Securities Act), relating to, any shares of our common stock or any securities convertible into or exchangeable or exercisable for any shares of our common stock, or publicly disclose the intention to make any offer, sale, pledge, disposition or filing, or (ii) enter into any swap or other arrangement that transfers all or a portion of the economic consequences associated with the ownership of any shares of our common stock or any such other securities (regardless of whether any of these transactions are to be settled by the delivery of shares of our common stock or such other securities, in cash or otherwise), in each case without the prior written consent of J.P. Morgan Securities LLC and Morgan Stanley & Co. LLC for a period of 180 days after the date of this prospectus, other than (i) the shares of our common stock to be sold hereunder, (ii) any shares of our common stock issued upon the exercise of options granted under our existing management incentive plans or warrants described as outstanding in the registration statement of which this prospectus forms a part, (iii) any options and other awards granted under an equity incentive plan described in the registration statement of which this prospectus forms a part, (iv) our filing of any registration statement on Form S-8 or a successor form thereto relating to an equity incentive plan described in the registration statement of which this prospectus forms a part, and (v) shares of common stock or other securities issued in connection with a transaction with an unaffiliated third party that includes a bona fide commercial relationship (including joint ventures, marketing or distribution arrangements, collaboration agreements or intellectual property license agreements) or any acquisition of assets or acquisition of not less than a majority or controlling portion of the equity of another entity, provided that (x) the aggregate number of shares issued pursuant to this clause (v) shall not exceed five percent (5%) of the total number of outstanding shares of common stock immediately following the issuance and sale of the shares of common stock in this offering and (y) the recipient of any such shares of common stock and securities issued pursuant to this clause (v) during the 180-day restricted period described above shall enter into a lock-up agreement.

Our directors and executive officers, and substantially all of our stockholders have entered into lock-up agreements with the underwriters prior to the commencement of this offering pursuant to which each of these persons or entities, with limited exceptions, for a period of 180 days after the date of this prospectus, may not, without the prior written consent of J.P. Morgan Securities LLC and Morgan Stanley & Co. LLC, (1) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, any shares of our common stock or any securities convertible into or exercisable or exchangeable for our common stock (including without limitation, common stock or such other securities which may be deemed to be beneficially owned by such directors, executive officers and shareholders in accordance with the rules and regulations of the Securities and Exchange Commission and securities which may be issued upon exercise of a stock option or warrant), or publicly disclose the intention to make any offer, sale, pledge or disposition, (2) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of our common stock or such other securities, whether any such transaction described in clause (1) or (2) above is to be settled by delivery of common stock or such other securities, in cash or otherwise or (3) make any demand for or exercise any right with respect to the registration of any shares of our common stock or any security convertible into or exercisable or exchangeable for our common stock. The restrictions described in the immediately preceding paragraph to do not apply to:

transfers or dispositions of shares of common stock (or any security convertible into or exercisable or exchangeable for common stock):

as a bona fide gift;

to any trust for the direct or indirect benefit of the party subject to the lock-up restrictions or the immediate family of such person;

to any corporation, partnership, limited liability company, investment fund or other entity controlled or managed, or under common control or management by the party subject to the lock-up restrictions or the immediate family of such person;

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by will, other testamentary document or intestate succession to the legal representative, heir, beneficiary or a member of the immediate family of the party subject to the lockup restrictions; and

as distributions to partners, members or stockholders of the party subject to the lock-up restrictions,

provided that in the case of any transfer or distribution pursuant to the above five subclauses, (i) each donee or distributee shall sign and deliver a lock-up letter substantially in the form executed by the party subject to the lock up restrictions and (ii) no filing under Section 16(a)of the Exchange Act, reporting a reduction in beneficial ownership of shares of common stock, shall be required or shall be voluntarily made during the restricted period (other than a filing on Form 5);

the establishment of a trading plan pursuant to Rule 10b5-1 under the Exchange Act for the transfer of shares of common stock, *provided* that (i) such plan does not provide for the transfer of common stock during the restricted period and (ii) no filing under the Exchange Act or other public announcement shall be required or voluntarily made by or on behalf of the party subject to the lock-up restrictions regarding the establishment of such plan;

the exercise of options to purchase shares of common stock granted under any stock incentive plan or stock purchase plan of the Company, *provided* that the underlying shares shall continue to be subject to the restrictions on transfer set forth in this agreement and *provided further* that no filing under Section 16(a) of the Exchange Act shall be required or shall be voluntarily made during the restricted period (other than a filing on Form 5);

the exercise (whether for cash, cashless, or net exercise) of warrants to purchase shares of common stock (or any security convertible into or exercisable or exchangeable for common stock), *provided* that the underlying shares shall continue to be subject to the lock-up restrictions and *provided further* that, other than in respect of warrants that will expire or automatically exercise by their terms in connection with this offering, no filing under Section 16(a) of the Exchange Act shall be required or shall be voluntarily made during the restricted period (other than a filing on Form 5);

the transfer of shares of common stock (or any security convertible into common stock) to the Company or sold in connection with a vesting event of the Company s securities or upon the exercise of options to purchase the Company s securities, on a cashless or net exercise basis or to cover tax withholding obligations of the party subject to the lock-up restrictions in connection with such vesting or exercise *provided* that no filing under Section 16(a) of the Exchange Act shall be required or shall be voluntarily made during the restricted period (other than a filing on Form 5);

the transfer or disposition of the shares of common stock (or any security convertible into or exercisable or exchangeable for common stock) held by the party subject to the lock-up restrictions that occurs by operation of law, such as pursuant to a qualified domestic order or in connection with a divorce settlement *provided* that each transferee shall sign and deliver a lock-up letter substantially in the form executed by the party subject to the lock-up restrictions;

the transfer of shares of common stock (or any security convertible into or exercisable or exchangeable for common stock) pursuant to a bona fide third party tender offer, merger, consolidation or other similar transaction made to all holders of the common stock involving a change of control of the Company, *provided* that in the event that the tender offer, merger, consolidation or other such transaction is not completed, the common stock owned by the party subject to the lock-up restrictions shall remain subject to such restrictions; or

transactions by any person other than us relating to shares of common stock or other securities acquired in open market transactions after the completion of the offering of the shares, *provided* that no filing under Section 16(a) of the Exchange Act is required or voluntarily made in connection with subsequent sales of the common stock or other securities acquired in such open market transactions (other than a filing on Form 5).

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We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act of 1933, as amended.

Our common stock has been approved for listing/quotation on The NASDAQ Global Select Market under the symbol RARE.

In connection with this offering, the underwriters may engage in stabilizing transactions, which involves making bids for, purchasing and selling shares of common stock in the open market for the purpose of preventing or retarding a decline in the market price of the common stock while this offering is in progress. These stabilizing transactions may include making short sales of the common stock, which involves the sale by the underwriters of a greater number of shares of common stock than they are required to purchase in this offering, and purchasing shares of common stock on the open market to cover positions created by short sales. Short sales may be covered shorts, which are short positions in an amount not greater than the underwriters option to purchase additional shares referred to above, or may be naked shorts, which are short positions in excess of that amount. The underwriters may close out any covered short position either by exercising their option to purchase additional shares, in whole or in part, or by purchasing shares in the open market. In making this determination, the underwriters will consider, among other things, the price of shares available for purchase in the open market compared to the price at which the underwriters may purchase shares through the option to purchase additional shares. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market that could adversely affect investors who purchase in this offering. To the extent that the underwriters create a naked short position, they will purchase shares in the open market to cover the position.

The underwriters have advised us that, pursuant to Regulation M of the Securities Act, they may also engage in other activities that stabilize, maintain or otherwise affect the price of the common stock, including the imposition of penalty bids. This means that if the representatives of the underwriters purchase common stock in the open market in stabilizing transactions or to cover short sales, the representatives can require the underwriters that sold those shares as part of this offering to repay the underwriting discount received by them.

These activities may have the effect of raising or maintaining the market price of the common stock or preventing or retarding a decline in the market price of the common stock, and, as a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. If the underwriters commence these activities, they may discontinue them at any time. The underwriters may carry out these transactions on The NASDAQ Global Select Market, in the over-the-counter market or otherwise.

Prior to this offering, there has been no public market for our common stock. The initial public offering price will be determined by negotiations between us and the representatives of the underwriters. In determining the initial public offering price, we and the representatives of the underwriters expect to consider a number of factors including:

- the information set forth in this prospectus and otherwise available to the representatives;
- our prospects and the history and prospects for the industry in which we compete;
- an assessment of our management;
- our prospects for future earnings;
- the general condition of the securities markets at the time of this offering;
- the recent market prices of, and demand for, publicly traded common stock of generally comparable companies; and
- other factors deemed relevant by the underwriters and us.

Neither we nor the underwriters can assure investors that an active trading market will develop for our common shares, or that the shares will trade in the public market at or above the initial public offering price.

At our request, the underwriters have reserved approximately up to 258,900 shares of our common stock offered by this prospectus for sale, at the initial public offering price, to our directors and officers and certain

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employees and other parties related to us. Shares purchased by our directors and officers will be subject to the 180-day lock-up restriction described above. The number of shares of common stock available for sale to the general public will be reduced to the extent these individuals purchase such reserved shares. Any reserved shares that are not so purchased will be offered by the underwriters to the general public on the same basis as the other shares offered by this prospectus.

Selling restrictions

General

Other than in the United States, no action has been taken by us or the underwriters that would permit a public offering of the securities offered by this prospectus in any jurisdiction where action for that purpose is required. The securities offered by this prospectus may not be offered or sold, directly or indirectly, nor may this prospectus or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus. This prospectus does not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus in any jurisdiction in which such an offer or a solicitation is unlawful.

United Kingdom

Each underwriter has represented and agreed that:

(1) it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the FSMA) received by it in connection with the issue or sale of our common shares in circumstances in which Section 21(1) of the FSMA does not apply to us; and

(2) it has complied and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to our common shares in, from or otherwise involving the United Kingdom.

European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a Relevant Member State), an offer to the public of any shares which are the subject of the offering contemplated by this prospectus (the Shares) may not be made in that Relevant Member State, except that an offer to the public in that Relevant Member State of any Shares may be made at any time under the following exemptions under the Prospectus Directive, if they have been implemented in that Relevant Member State:

(1) to any legal entity which is a qualified investor as defined in the Prospectus Directive;

(2) to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representatives for any such offer; or

(3) in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of Shares shall result in a requirement for the publication by us or any underwriter of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an offer to the public in relation to any Shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and any Shares to be offered so as to enable an investor to decide to purchase any Shares, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State, the expression Prospectus Directive means Directive 2003/71/EC (and amendments thereto,

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including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State), and includes any relevant implementing measure in the Relevant Member State, and the expression 2010 PD Amending Directive means Directive 2010/73/EU.

Switzerland

The shares may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or the SIX, or on any other stock exchange or regulated trading facility in Switzerland. This document has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this prospectus nor any other offering or marketing material relating to the shares or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this prospectus nor any other offering or marketing material relating to the offering, the Company, the shares have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of shares will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA, and the offer of shares has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or the CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of shares.

Hong Kong

The shares may not be offered or sold by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap.32, Laws of Hong Kong), or (ii) to professional investors within the meaning of the Securities and Futures Ordinance (Cap.571, Laws of Hong Kong) and any rules made thereunder, or (iii) in other circumstances which do not result in the document being a prospectus within the meaning of the Companies Ordinance (Cap.32, Laws of Hong Kong), and no advertisement, invitation or document relating to the shares may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to professional investors within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder.

Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the SFA), (ii) to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the shares are subscribed or purchased under Section 275 by a relevant person which is: (a) a corporation (which is not an accredited investor) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or (b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary is an accredited investor, shares, debentures and units of shares and debentures of that corporation or the beneficiaries rights and interest in that trust shall not be transferable for 6 months after that corporation or that trust has acquired the shares under Section 275 except: (1) to an institutional investor under Section 274 of the SFA or to a relevant

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person, or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the SFA; (2) where no consideration is given for the transfer; or (3) by operation of law.

Japan

The securities have not been and will not be registered under the Financial Instruments and Exchange Law of Japan (the Financial Instruments and Exchange Law) and each underwriter has agreed that it will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the Financial Instruments and Exchange Law and any other applicable laws, regulations and ministerial guidelines of Japan.

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LEGAL MATTERS

The validity of the issuance of our common stock offered in this prospectus will be passed upon for us by Ropes & Gray LLP, San Francisco, California. Certain legal matters in connection with this offering will be passed upon for the underwriters by Latham & Watkins LLP, Costa Mesa, California.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our financial statements at December 31, 2011 and 2012, and for each of the two years in the period ended December 31, 2012, and for the period from April 22, 2010 (Inception) to December 31, 2012, as set forth in their report. We have included our financial statements in the prospectus and elsewhere in the registration statement in reliance on Ernst & Young LLP s report, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-1, or the registration statement, under the Securities Act with respect to the shares of common stock offered hereby. This prospectus, which constitutes a part of the registration statement, does not contain all of the information set forth in the registration statement or the exhibits and schedules filed therewith. For further information with respect to Ultragenyx Pharmaceutical Inc. and the common stock offered hereby, reference is made to the registration statement and the exhibits and schedules filed therewith. Statements contained in this prospectus regarding the contents of any contract or any other document that is filed as an exhibit to the registration statement are not necessarily complete, and each such statement is qualified in all respects by reference to the full text of such contract or other document filed as an exhibit to the registration statement. A copy of the registration statement and the exhibits and schedules filed therewith may be inspected without charge at the public reference room maintained by the SEC, located at 100 F Street N.E., Washington, D.C. 20549, and copies of all or any part of the registration statement may be obtained from such offices upon the payment of the fees prescribed by the SEC. Please call the SEC at 1-800-SEC-0330 for further information about the public reference room. The SEC also maintains a website that contains reports, proxy and information statements and other information regarding registrants that file electronically with the SEC. The address is www.sec.gov.

Upon completion of this offering, we will become subject to the information and periodic reporting requirements of the Exchange Act and, in accordance therewith, will file periodic reports, proxy statements and other information with the SEC. Such periodic reports, proxy statements and other information will be available for inspection and copying at the public reference room and website of the SEC referred to above. We maintain a website at *www.ultragenyx.com*. The reference to our website address does not constitute incorporation by reference of the information contained on our website, and you should not consider the contents of our website in making an investment decision with respect to our common stock.

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

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Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of

Ultragenyx Pharmaceutical Inc.

We have audited the accompanying balance sheets of Ultragenyx Pharmaceutical Inc. (a development stage company) (the Company) as of December 31, 2011 and 2012, and the related statements of operations and comprehensive loss, convertible preferred stock and stockholders deficit, and cash flows for each of the two years in the period ended December 31, 2012, and for the period from April 22, 2010 (Inception) through December 31, 2012. These financial statements are the responsibility of the Company s management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company s internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company s internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Ultragenyx Pharmaceutical Inc. at December 31, 2011 and 2012, and the results of its operations and comprehensive loss and its cash flows for each of the two years in the period ended December 31, 2012 and for the period from April 22, 2010 (Inception) through December 31, 2012, in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP

Redwood City, California

October 3, 2013, except for the last paragraph of Note 2, as to which the date is January 17, 2014

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

BALANCE SHEETS

(In thousands, except share and per share amounts)

	December 31, 2011	2012
Assets		
Current assets:		
Cash and cash equivalents	$ 10,645	$ 86,190
Receivables due from related party	103	
Prepaid expenses and other current assets	205	255
Total current assets	10,953	86,445
Property and equipment, net	759	1,362
Restricted cash	376	476
Other assets	41	33
Total assets	$ 12,129	$ 88,316
Liabilities, Convertible Preferred Stock and Stockholders Deficit		
Current liabilities:		
Accounts payable	$ 342	$ 1,200
Accrued liabilities	657	1,913
Deferred rent current portion		75
Total current liabilities	999	3,188
Convertible preferred stock warrant liability	216	518
Other liabilities	271	270
Total liabilities	1,486	3,976
Commitments and contingencies (Note 6)		
Series A redeemable convertible preferred stock, par value of $0.001 per share 62,000,000 and 35,377,556 shares authorized as of December 31, 2011 and 2012; 18,052,464 and 34,349,894 shares issued and outstanding as of December 31, 2011 and 2012; redemption value of $47,159 as of December 31, 2012	18,604	37,458
Series B convertible preferred stock, par value of $0.001 per share 0 and 27,081,680 shares authorized as of December 31, 2011 and 2012; 0 and 27,081,680 shares issued and outstanding as of December 31, 2011 and 2012; aggregate liquidation preference of $75,060 as of December 31, 2012		73,929
Stockholders deficit:		
Common stock, par value of $0.001 per share 85,000,000 shares authorized; 3,038,620 and 3,458,928 shares issued and outstanding as of December 31, 2011 and 2012	3	3
Additional paid-in capital	191	8
Deficit accumulated during the development stage	(8,155)	(27,058)
Total stockholders deficit	(7,961)	(27,047)
Total liabilities, convertible preferred stock and stockholders deficit	$ 12,129	$ 88,316

See accompanying notes.

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

(In thousands, except share and per share amounts)

	Year Ended December 31,		Period from April 22, 2010 (Inception) Through December 31,
	2011	2012	2012
Operating expenses:			
Research and development	$ 4,717	$ 12,641	$ 18,316
General and administrative	1,844	3,344	5,480
Total operating expenses	6,561	15,985	23,796
Loss from operations	(6,561)	(15,985)	(23,796)
Other income (expense), net:			
Interest income	4	1	5
Interest expense	(270)		(318)
Other expense, net	(22)	(350)	(380)
Total other income (expense), net	(288)	(349)	(693)
Net loss and comprehensive loss	$ (6,849)	$ (16,334)	$ (24,489)
Net loss attributable to common stockholders	$ (7,466)	$ (19,561)	
Net loss per share attributable to common stockholders, basic and diluted	$ (4.62)	$ (14.20)	
Shares used in computing net loss per share attributable to common stockholders, basic and diluted	1,617,384	1,377,207	
Pro forma net loss per share attributable to common stockholders, basic and diluted (unaudited)		$ (2.04)	
Shares used in computing pro forma net loss per share attributable to common stockholders, basic and diluted (unaudited)		9,935,836	

See accompanying notes.

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

STATEMENTS OF CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS DEFICIT

(In thousands, except share and per share amounts)

	Convertible Preferred Stock						Stockholders Deficit		
	Series A Redeemable Convertible Preferred Stock		Series B Convertible Preferred Stock		Common Stock				
	Shares	Amount	Shares	Amount	Shares	Amount	Additional Paid-In Capital	Deficit Accumulated During the Development Stage	Total Stockholders Deficit
Balance as of April 22, 2010 (Inception)		$		$		$	$	$	$
Issuance of common stock for cash					2,628,808	3	(2)		1
Net loss and comprehensive loss								(1,306)	(1,306)
Balance as of December 31, 2010					2,628,808	3	(2)	(1,306)	(1,305)
Issuance of common stock for cash					409,812				
Issuance of Series A redeemable convertible preferred stock for cash at $1.034 per share, net of $121 of issuance cost in June 2011	14,508,173	14,879							
Issuance of Series A redeemable convertible preferred stock in exchange for conversion of promissory notes and accrued interest at $1.034 per share in June 2011	3,544,291	3,664							
Stock-based compensation expense related to employee stock option grants							36		36
Stock-based compensation expense related to founder s stock							218		218
Accretion on convertible preferred stock		61					(61)		(61)
Net loss and comprehensive loss								(6,849)	(6,849)
Balance as of December 31, 2011	18,052,464	18,604			3,038,620	3	191	(8,155)	(7,961)
Issuance of common stock upon exercise of stock options					420,308		131		131
Issuance of Series A redeemable convertible preferred stock for cash at	14,604,895	15,080							

$1.034 per share, net of $20 of issuance cost in July 2012									
Issuance of Series A redeemable convertible preferred stock in lieu of cash dividend	1,692,535	2,070					(1,205)	(865)	(2,070)
Issuance of Series B convertible preferred stock for cash at $2.77 per share, net of $1,071 of issuance cost in December 2012			27,081,680	73,929					
Stock-based compensation expense related to employee stock option grants							178		178
Stock-based compensation expense related to founder s stock							713		713
Accretion on convertible preferred stock		1,704						(1,704)	(1,704)
Net loss and comprehensive loss								(16,334)	(16,334)
Balance as of December 31, 2012	34,349,894	$ 37,458	27,081,680	$ 73,929	3,458,928	$ 3	$ 8	$ (27,058)	$ (27,047)

See accompanying notes.

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

STATEMENTS OF CASH FLOWS

(In thousands)

	Year Ended December 31,		Period from April 22, 2010 (Inception) Through December 31, 2012
	2011	2012	
Operating activities:			
Net loss	$ (6,849)	$ (16,334)	$ (24,489)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	34	313	353
Noncash interest expense	270		318
Stock-based compensation	254	891	1,145
Revaluation of convertible preferred stock warrant liability	13	302	315
Changes in operating assets and liabilities:			
Receivable related party	(3)	3	
Prepaid expenses and other current assets	(205)	(50)	(255)
Other assets	(41)	8	(33)
Accounts payable	252	858	1,200
Accrued expenses and other liabilities	450	1,505	2,257
Net cash used in operating activities	(5,825)	(12,504)	(19,189)
Investing activities:			
Purchase of property and equipment	(548)	(1,091)	(1,715)
Increase in restricted cash	(376)	(100)	(476)
Net cash used in investing activities	(924)	(1,191)	(2,191)
Financing activities:			
Net proceeds from issuance of convertible preferred stock	14,879	89,009	103,888
Net proceeds from issuance of common stock		131	132
Proceeds from issuance of promissory notes	2,450	100	3,550
Net cash provided by financing activities	17,329	89,240	107,570
Net increase in cash and cash equivalents	10,580	75,545	86,190
Cash and cash equivalents at beginning of period	65	10,645	
Cash and cash equivalents at end of period	$ 10,645	$ 86,190	$ 86,190
Supplemental disclosures of non-cash investing and financing information:			
Issuance of convertible preferred stock warrants	$ 157	$	$ 202
Issuance of Series A redeemable convertible preferred stock in lieu of cash dividend	$	$ 2,070	$ 2,070

Conversion of promissory notes into Series A redeemable convertible preferred stock	$ 3,550	$	$ 3,550
Conversion of interest accrued on promissory notes into Series A redeemable convertible preferred stock	$ 114	$	$ 114

See accompanying notes.

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

Notes to Financial Statements

1. Organization and Basis of Presentation

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

The Company is focused on the identification, acquisition, development, and commercialization of novel products for the treatment of rare and ultra-rare diseases, with an initial focus on serious, debilitating metabolic genetic diseases. The Company is currently conducting a Phase 2 clinical trial of sialic acid, extended release (SA-ER) in patients with hereditary inclusion body myopathy (HIBM), a progressive muscle-wasting disorder. The Company is in the development stage as of December 31, 2012, as defined by Financial Accounting Standards Board (FASB) Accounting Standards Codification (ASC) 915, *Development Stage Entities*, and since Inception has been engaged in developing its product candidates, raising capital and recruiting personnel. The Company operates in one reportable segment in the United States of America.

In the course of its development activities, the Company has sustained operating losses and expects such losses to continue over the next several years. The Company s ultimate success depends on the outcome of its research and development activities. From April 22, 2010 (Inception) through December 31, 2012, the Company has incurred cumulative net losses of $24.5 million. Management expects to incur additional losses in the future to conduct product research and development and recognizes the need to raise additional capital to fully implement its business plan. The Company intends to raise such capital through the issuance of additional equity, and potentially through borrowings, and strategic alliances with partner companies. However, if such financing is not available at adequate levels, the Company will need to reevaluate its operating plans.

2. Summary of Significant Accounting Policies

Use of Estimates

The accompanying financial statements have been prepared in accordance with U.S. generally accepted accounting principles (GAAP). The preparation of the financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, disclosure of contingent liabilities and the reported amounts of expenses in the financial statements and the accompanying notes. On an ongoing basis, management evaluates its estimates, including those related to clinical trial accruals, fair value of assets and liabilities, convertible preferred stock and related warrants, common stock, income taxes and stock-based compensation. Management bases its estimates on historical experience and on various other market-specific and relevant assumptions that management believes to be reasonable under the circumstances. Actual results could differ from those estimates.

Cash and Cash Equivalents

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

Restricted Cash

Restricted cash consists of a money market account with one of the Company s financial institutions as collateral for its obligations under its facility lease of the Company s corporate headquarters in Novato, California. Additionally, restricted cash includes a savings account associated with a credit card agreement at one of the Company s financial institutions.

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

Notes to Financial Statements (continued)

2. Summary of Significant Accounting Policies (continued)

Concentration of Credit Risk

Financial instruments that potentially subject the Company to a concentration of credit risk consist of cash and cash equivalents. The Company s cash and cash equivalents are held by two financial institutions in the United States. Such deposits may exceed federally insured limits. Management believes that these financial institutions are financially sound, and, accordingly, minimal credit risk exists with respect to those financial institutions. The Company is exposed to credit risk in the event of default by the financial institutions holding its cash and cash equivalents to the extent recorded in the balance sheets.

Fair Value Measurement

Fair value accounting is applied for all financial assets and liabilities and non-financial assets and liabilities that are recognized or disclosed at fair value in the financial statements on a recurring basis (at least annually).

Property and Equipment

Property and equipment are stated at cost, less accumulated depreciation and amortization. Depreciation is computed using the straight-line method over the estimated useful lives of the respective assets. Depreciation begins at the time the asset is placed in service. Maintenance and repairs are charged to operations as incurred. Upon sale or retirement of assets, the cost and related accumulated depreciation are removed from the balance sheet and the resulting gain or loss, if any, is reflected in operations.

The useful lives of the property and equipment are as follows:

Research and development equipment	5 years
Furniture and office equipment	5 years
Computer equipment	3 years
Software	3 years
Leasehold improvements	Shorter of lease term or estimated useful life

Impairment of Long-Lived Assets

The Company evaluates its long-lived assets, including property and equipment, for impairment whenever events or changes in circumstances indicate that the carrying value of these assets may not be recoverable. Recoverability of these assets is measured by comparison of the carrying amount of each asset to the future undiscounted cash flows expected to result from the use of the asset and its eventual disposition. If the asset is considered to be impaired, the amount of any impairment is measured as the difference between the carrying value and the fair value of the impaired asset. The Company has not recorded impairment of any long-lived assets since inception.

Accruals of Research and Development Costs

The Company records accruals for estimated costs of research, preclinical and clinical studies and manufacturing development. These costs are a significant component of the Company s research and development expenses. A substantial portion of the Company s ongoing research and development activities are conducted by third-party service providers, including contract research organizations. The Company accrues the costs incurred under its agreements with these third parties based on actual work completed in accordance with

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

Notes to Financial Statements (continued)

2. Summary of Significant Accounting Policies (continued)

agreements established with these third parties. The Company determines the actual costs through discussions with internal personnel and external service providers as to the progress or stage of completion of the services and the agreed-upon fee to be paid for such services. The Company makes significant judgments and estimates in determining the accrual balance in each reporting period. As actual costs become known, the Company adjusts its accruals. The Company has not experienced any material deviations between accrued clinical trial expenses and actual clinical trial expenses. However, actual services performed, number of patients enrolled, and the rate of patient enrollment may vary from the Company s estimates, resulting in adjustments to clinical trial expense in future periods. Changes in these estimates that result in material changes to the Company s accruals could materially affect the Company s results of operations.

Leases

The Company enters into lease agreements for its office and laboratory facilities. These leases are classified as operating leases. Rent expense is recognized on a straight-line basis over the term of the lease and, accordingly, the Company records the difference between cash rent payments and the recognition of rent expense as a deferred rent liability. Incentives granted under the Company s facilities leases, including allowances to fund leasehold improvements, are deferred and are recognized as adjustments to rental expense on a straight-line basis over the term of the lease.

Convertible Preferred Stock

The Company initially records all shares of convertible preferred stock net of offering costs on the dates of issuance, which represents the carrying value. At any time after June 16, 2017, but within sixty (60) days after the receipt by the Company of a written request from the holders of not less than seventy-five percent (75%) of the then outstanding Series A convertible preferred stock, all shares of Series A convertible preferred stock can be redeemed. As only the passage of time is required for Series A convertible preferred stock to become redeemable, the Company is accreting the carrying value of Series A convertible preferred stock to its redemption value over the period from the date of issuance to June 16, 2017 (the earliest redemption date). In the event of a change of control of the Company, proceeds will be distributed in accordance with the liquidation preferences set forth in its Amended and Restated Certificate of Incorporation unless the holders of convertible preferred stock have converted their convertible preferred shares into common shares. Therefore, convertible preferred stock is classified outside of stockholders deficit on the accompanying balance sheets, as Series A convertible preferred stock can be redeemed and as events triggering the liquidation preferences are not solely within the Company s control.

Convertible Preferred Stock Warrant Liability

Warrants for shares that are either puttable or that are contingently redeemable are classified as liabilities on the balance sheets. The warrants are subject to remeasurement at each balance sheet date, with changes in fair value recognized as a component of interest and other expense. The Company will continue to adjust the liability for changes in fair value until the earlier of the expiration of the warrants, exercise of the warrants, or conversion of the warrants upon the completion of a liquidation event, including the completion of an initial public offering to common stock warrants that will no longer be subject to remeasurement.

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

Notes to Financial Statements (continued)

2. Summary of Significant Accounting Policies (continued)

Research and Development

Research and development costs are expensed as incurred and consist of salaries and benefits, stock-based compensation expense, lab supplies and facility costs, as well as fees paid to other nonemployees and entities that conduct certain research and development activities on the Company s behalf. Amounts incurred in connection with license agreements are also included in research and development expense. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

Stock-Based Compensation

Stock-based awards issued to employees, including stock options, are recorded at fair value as of the grant date using the Black-Scholes option-pricing model and recognized as expense on a straight-line basis over the employee s requisite service period (generally the vesting period). Because noncash stock compensation expense is based on awards ultimately expected to vest, it is reduced by an estimate for future forfeitures. Forfeitures are estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from estimates.

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 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.

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

Notes to Financial Statements (continued)

2. Summary of Significant Accounting Policies (continued)

Unaudited Pro Forma Net Loss per Share Attributable to Common Stockholders

Pro forma basic and diluted net loss per share attributable to common stockholders has been computed to give effect to the conversion of the convertible preferred stock into common stock in connection with the Company s initial public offering. Also, the numerator in the pro forma basic and diluted net loss per share attributable to common stockholders calculation has been adjusted to remove gains and losses resulting from remeasurement of the convertible preferred stock warrant liability as these amounts will be reclassified to additional paid-in capital upon a qualifying initial public offering of the Company s common stock and has also been adjusted to reflect the payment of a dividend to the Company s convertible preferred stockholders concurrent with the conversion of the Company s convertible preferred stock to common stock immediately prior to the completion of this offering. The denominator in the pro forma basic and diluted net loss per share attributable to common stockholders has been adjusted to give effect to the number of shares that would be required to be issued at an initial public offering price of $21.00 per share to pay the dividend to the convertible preferred stockholders. The pro forma net loss per share attributable to common stockholders does not include the shares expected to be sold and related proceeds to be received from the initial public offering.

Recent Accounting Pronouncements

In February 2013, the FASB issued Accounting Standards Update (ASU) No. 2013-02, *Other Comprehensive Income (Topic 220): Reporting of Amounts Reclassified Out of Accumulated Other Comprehensive Income*. ASU No. 2013-02 supersedes the presentation requirements for reclassifications out of accumulated other comprehensive income in ASU 2011-05 and 2011-12 and requires an entity to provide additional information about reclassifications out of accumulated other comprehensive income. The amendment is effective in fiscal years beginning after December 15, 2012. The adoption of this amendment will not have a material impact on the Company s results of operations or financial position.

Reverse Stock Split

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

3. Fair Value Measurements

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

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

Notes to Financial Statements (continued)

3. Fair Value Measurements (continued)

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 Company s financial instruments consist of Level 1 assets and Level 3 liabilities. Where quoted prices are available in an active market, securities are classified as Level 1. Level 1 assets consist primarily of highly liquid money market funds that are included in restricted cash.

In certain cases where there is limited activity or less transparency around inputs to valuation, securities are classified as Level 3. Level 3 liabilities consist of the convertible preferred stock warrant liability. The following table sets 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):

	December 31, 2011			
	Level 1	Level 2	Level 3	Total
Financial Assets:				
Money market funds	$ 376	$	$	$ 376
Total financial assets	$ 376	$	$	$ 376
Financial Liabilities:				
Convertible preferred stock warrant liability	$	$	$ 216	$ 216
Total financial liabilities	$	$	$ 216	$ 216

	December 31, 2012			
	Level 1	Level 2	Level 3	Total
Financial Assets:				
Money market funds	$ 376	$	$	$ 376
Total financial assets	$ 376	$	$	$ 376
Financial Liabilities:				

Convertible preferred stock warrant liability	$	$	$ 518	$ 518
Total financial liabilities	$	$	$ 518	$ 518

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

Notes to Financial Statements (continued)

3. Fair Value Measurements (continued)

The following table sets forth a summary of the changes in the fair value of the Company s Level 3 financial liabilities (in thousands):

	Year Ended December 31,	
	2011	2012
Fair value, beginning of period	$ 46	$ 216
Issuance of preferred stock warrants	157	
Change in fair value recorded as a loss in other expense, net	13	302
Fair value, end of period	$ 216	$ 518

The determination of the fair value of the convertible preferred stock warrants is discussed in Note 9. Generally, increases or decreases in the fair value of the underlying convertible preferred stock would result in a directionally similar impact in the fair value measurement of the warrant liability.

4. Balance Sheet Components

Property and Equipment, net

Property and equipment, net consists of the following (in thousands):

	December 31,	
	2011	2012
Research and development equipment	$ 128	$ 225
Furniture and office equipment	80	266
Computer equipment	52	187
Software	10	34
Leasehold improvements	529	1,003
Property and equipment, gross	799	1,715
Less accumulated depreciation and amortization	(40)	(353)
Property and equipment, net	$ 759	$ 1,362

Depreciation and amortization expense for the years ended December 31, 2011 and 2012 and the period from April 22, 2010 (Inception) through December 31, 2012 was $34,000, $313,000 and $353,000, respectively.

Accrued Liabilities

Accrued liabilities consist of the following (in thousands):

	December 31,	
	2011	2012
Research and clinical trial expenses	$ 147	$ 595
Payroll and related expenses	419	1,289
Other	91	29
Total accrued liabilities	$ 657	$ 1,913

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

Notes to Financial Statements (continued)

5. Convertible Promissory Notes

In June 2010, the Company entered into a convertible promissory note and warrant purchase agreement with its Chief Executive Officer and Founder, Emil Kakkis, M.D., PhD, in which it could borrow up to $1,000,000 from Dr. Kakkis at an interest rate of 8% per annum. During 2010, the Company borrowed the entire amount of $1,000,000 available under the agreement. The note also contained a provision under which all outstanding principal and accrued interest would automatically be converted into preferred stock upon a financing event in which the Company issued newly authorized shares of preferred stock for aggregate proceeds of not less than $500,000. Under the terms of the agreement, the note automatically converted at the same terms and conditions of the financing. Pursuant to the agreement, the Company also issued a warrant to purchase shares of Series A convertible preferred stock (see Note 9). From July 2010 to June 2011, the Company entered into two additional convertible promissory note and warrant purchase agreements with Dr. Kakkis in which it borrowed an additional $800,000 under similar terms and issued additional warrants. In June 2011, the outstanding principal balance of $1,800,000 from all three notes plus accrued interest was converted into shares of Series A convertible preferred stock at the same issuance price per share of $1.034 as all other purchasers of Series A convertible preferred stock. The number of shares underlying the warrant to be issued was dependent on the aggregate amount owing at the time of the initial closing of the Series A convertible preferred stock financing and the price per share of the Series A convertible preferred stock. Based on the formula specified in the Warrant Agreement, warrants to purchase an aggregate of 435,245 shares of Series A convertible preferred stock at an exercise price of $1.034 were issued to Dr. Kakkis upon the initial closing in June 2011.

In February 2011, the Company entered into two note and warrant purchase agreements with two related parties in which it borrowed a total of $1,750,000 at an interest rate of 8% per annum. The notes and all accrued interest were fully due and payable on the one-year anniversary date of each respective note agreement. The notes also contained a provision under which all outstanding principal and accrued interest would automatically be converted into preferred stock upon a financing event in which the Company issued newly authorized shares of preferred stock for aggregate proceeds of not less than $500,000. Under the terms of the agreement, the notes automatically converted at the same terms and conditions of the financing. In June 2011, the outstanding principal balance of $1,750,000 plus accrued interest from the two notes was converted into shares of Series A convertible preferred stock at the same issuance price per share of $1.034 paid by all other purchasers of Series A convertible preferred stock. Pursuant to the agreement, the Company issued a warrant to purchase shares of Series A convertible preferred stock (see Note 9). The number of shares underlying the warrant to be issued was dependent on the aggregate amount of principal outstanding at the time of the initial closing of the Series A convertible preferred stock financing, subsequently completed in June 2011, and the price per share of the Series A convertible preferred stock. Based on the formula specified in the Warrant Agreements, warrants to purchase an aggregate of 592,417 shares of Series A convertible preferred stock at an exercise price of $1.034 were issued to the two note holders upon the closing of the financing in June 2011.

6. Commitments and Contingencies

Facilities

From inception until March of 2012, the Company rented office space in a building under an informal monthly agreement. The Company s founder also rented space for one of his other business interests in that same building.

In July 2011, the Company entered into a lease agreement for office facilities in Novato, California, which provided for a tenant improvement allowance of up to $376,000. The lease commenced in March of 2012. This noncancelable operating lease expires five years after the commencement date. At the end of the lease term, the

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

Notes to Financial Statements (continued)

6. Commitments and Contingencies (continued)

Company has the option to extend the lease for two additional consecutive terms of five years. The Company also signed an addendum to the lease agreement in July 2011 to add warehouse space to the arrangement.

In September 2010, the Company entered into a license and service agreement for a lab facility in Novato, California. The term commenced in September 2010. This agreement expires two years after the commencement date, and either party may terminate the agreement with one year s prior notice without cause and purely out of convenience of such party. In September 2012, the Company entered into an amendment to increase the size of the lab facility and extend the term. This amendment expires two years after the amendment date, and either party may terminate the agreement with one year s prior notice without cause.

As of December 31, 2012, the aggregate future minimum lease payments under the noncancelable operating lease arrangements are as follows (in thousands):

Year Ending December 31:	
2013	$ 345
2014	285
2015	285
2016	285
2017	47
	$ 1,247

The Company recognizes rent expense on a straight-line basis over the noncancelable term of its operating lease. Rent expense was $84,000, $265,000 and $367,000 during the years ended December 31, 2011 and 2012 and the period from April 22, 2010 (Inception) through December 31, 2012, respectively.

Under the terms of the lease agreement of its Novato office facility, the Company provided the lessor with an irrevocable letter of credit in the amount of $376,000. The lessor shall be entitled to draw on the letter of credit in the event of any uncured default by the Company under the terms of the lease. Provided there has been no default on the lease, the Company may reduce the amount of the letter of credit by $75,000 on each anniversary date from the commencement date.

Other Commitments

The Company has various manufacturing, clinical, research, and other contracts with vendors in the conduct of the normal course of its business. All contracts are terminable, with varying provisions regarding termination. If a contract with a specific vendor were to be terminated, the Company would only be obligated for the products or services that the Company had received at the time the termination became effective.

Contingencies

While there are no legal proceedings the Company is aware of, the Company may become party to various claims and complaints arising in the ordinary course of business. Management does not believe that any ultimate liability resulting from any of these 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 these claims, and their resolution could be material to operating results for any particular period, depending upon the level of income for the period.

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

Notes to Financial Statements (continued)

6. Commitments and Contingencies (continued)

Guarantees and Indemnifications

The Company indemnifies each of its directors for certain events or occurrences, subject to certain limits, while the director is or was serving at the Company s request in such capacity, as permitted under Delaware law and in accordance with its certificate of incorporation and bylaws. The term of the indemnification period lasts as long as a director may be subject to any proceeding arising out of acts or omissions of such director in such capacity. The maximum amount of potential future indemnification is unlimited; however, the Company currently holds director liability insurance. This insurance allows the transfer of risk associated with the Company s exposure and may enable it to recover a portion of any future amounts paid. The Company believes that the fair value of these indemnification obligations is minimal. Accordingly, it has not recognized any liabilities relating to these obligations for any period presented.

7. License and Research Agreements

Nobelpharma License Agreement

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

Under the collaboration and license agreement, the Company paid Nobelpharma $110,500 (10 million Yen) for the license, which was recorded as research and development expense in 2010, and also issued 76,567 shares of common stock to Nobelpharma with a minimal value. The Company is required to pay Nobelpharma annual royalties and earned royalties based on net sales upon product sales commencement. In addition, the Company is required to make certain payments to Nobelpharma based upon achievement of certain development and approval milestones. The Company paid $495,000 in development milestone payments from inception through December 31, 2012. The remaining total aggregate payments, if all milestones are achieved by Nobelpharma, would be 200 million Yen (approximately $2.3 million based on the exchange rate at December 31, 2012). The Company will pay a high single digit royalty on net sales in the Company s territory and will receive a mid-single digit royalty on net sales in the Nobelpharma territory, excluding Japan, if such product sales are ever achieved. Net sales, as defined in the collaboration and license agreement, represent the net sales of products whereby the licensed compound is the active ingredient. If the products include other active ingredients, the portion of the net sales allocated to the licensed compound would be used in determining the royalty payments.

Saint Louis University License Agreement

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

Under the license agreement, the Company paid SLU an up-front fee of $10,000, which was recorded as research and development expense in 2010. The Company will be required to make a milestone payment of $100,000 upon approval of a glucuronidase-based enzyme therapy for treatment of MPS 7. Additionally, upon

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

Notes to Financial Statements (continued)

7. License and Research Agreements (continued)

reaching a certain level of cumulative worldwide sales of the product, the Company will be required to pay to SLU a low single-digit royalty on net sales of the licensed products in any country or region, if such product sales are ever achieved.

AAI Pharma License Agreement

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

HIBM Research Group

License Agreement

In April 2012, the Company entered into an exclusive license agreement with HIBM Research Group (HRG). Under the terms of this license agreement, HRG granted the Company an exclusive worldwide license to certain intellectual property related to the treatment of HIBM.

Under the license agreement, the Company paid HRG an up-front fee of $25,000, which was recorded as research and development expense during the year ended December 31, 2012. The Company may make future payments that aggregate up to $300,000 and that are contingent upon attainment of various development and approval milestones. Additionally, the Company will pay to HRG a royalty of less than 1% of net sales of the licensed products in the licensed territories, if such product sales are ever achieved.

Research Agreement

In April 2012, the Company entered into a research agreement with HRG. Under the terms of this research agreement, the Company will engage HRG to perform certain nonclinical research activities related to the treatment for HIBM.

Under the research agreement, the Company was required to pay HRG an annual grant of $25,000 during the first five years from the effective date of the agreement. The agreement was terminated in 2013, and accordingly, no further amounts will be paid to HRG for research.

St. Jude Children s Research Hospital License Agreement

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

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

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

Notes to Financial Statements (continued)

7. License and Research Agreements (continued)

Baylor Research Institute License Agreement

In September 2012, the Company entered into a license agreement with Baylor Research Institute (BRI). Under the terms of this license agreement, BRI exclusively licensed to the Company certain intellectual property related to triheptanoin for North America.

Under the license agreement, the Company paid BRI an up-front fee of $250,000 which was recorded as research and development expense during the year ended December 31, 2012. 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.

The Company has an exclusive option to expand the licensed territory to a worldwide license if the previous holder of such territorial rights allows that option to lapse. The previous holder s option lapsed on December 31, 2012, and on June 26, 2013, the Company notified BRI that it was exercising its exclusive option to expand the licensed territory. The fee associated with this option exercise is $750,000 See Note 15- Subsequent Events.

8. Related Party Transactions

Emil Kakkis, M.D., Ph.D., Founder, member of the Company s Board of Directors, President, and Chief Executive Officer, entered into a Note and Warrant Purchase Agreement with the Company whereby Dr. Kakkis loaned the Company a total of $1,800,000. In June 2011, the outstanding principal balance of $1,800,000 and all accrued interest was converted into Series A convertible preferred stock at the same issuance price of $1.034 paid by all other purchasers of Series A convertible preferred stock. As per the Note and Warrant Purchase Agreement, the Company issued Dr. Kakkis a warrant to purchase 435,245 shares of Series A convertible preferred stock with an exercise price of $1.034 per share.

William Aliski, a member of the Company s Board of Directors, entered into a Note and Warrant Purchase Agreement with the Company whereby Mr. Aliski loaned the Company $250,000 in February 2011. In June 2011, the outstanding principal balance of $250,000 and all accrued interest was converted into shares of Series A convertible preferred stock at the same issuance price of $1.034 paid by all other purchasers of Series A convertible preferred stock. As per the Note and Warrant Purchase Agreement, the Company issued Mr. Aliski a warrant to purchase 84,631 shares of Series A convertible preferred stock with an exercise price of $1.034 per share.

John Klock, a former member and current observer of the Company s Board of Directors, entered into a Note and Warrant Purchase Agreement with the Company whereby Mr. Klock loaned the Company $1,500,000 in February 2011. In June 2011, the outstanding principal balance of $1,500,000 and all accrued interest was converted into shares of Series A convertible preferred stock at the same issuance price of $1.034 paid by all other purchasers of Series A convertible preferred stock. As per the Note and Warrant Purchase Agreement, the Company issued Mr. Klock a warrant to purchase 507,786 shares of Series A convertible preferred stock with an exercise price of $1.034 per share.

From the inception of the Company to March 2012, the Company rented its office facility in Novato, California, from an entity affiliated with Dr. Kakkis. Rent expense under this arrangement was $92,000 for the period from April 22, 2010 (Inception) through December 31, 2012.

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

Notes to Financial Statements (continued)

9. Convertible Preferred Stock Warrants

In connection with the terms of various promissory notes issued by the Company from June 2010 through February 2011, the Company issued warrants in which the number of shares and exercise price were subject to the per share price offered in the Series A convertible preferred stock sale. In June 2011, in connection with its closing of the first round of Series A convertible preferred stock financing, the Company determined that the warrants were convertible to 1,027,662 shares of Series A convertible preferred stock at an exercise price of $1.034 per share. The warrants expire on the earlier of (i) change of control of the Company or any simultaneous sale of more than a majority of the then-outstanding securities of the Company other than a mere reincorporation transaction or (ii) the ten year anniversary of their issue date. The Company determined the fair value of the warrants using an option-pricing method to allocate the equity value of the Company to the warrants based on the Company s capital structure. The equity value was estimated using the Back-Solve method, whereby the equity value was derived from a recent transaction involving the Company s own securities. The fair value ascribed to these warrants upon their issuance was $203,000. The fair value of the warrants was recorded as debt issuance costs and was amortized to interest expense using the effective-interest-rate method over the loan term. In connection with the conversion of the promissory notes into shares of Series A convertible preferred stock in June 2011, the Company recognized all remaining unamortized debt issuance costs.

As of December 31, 2011 and 2012, outstanding warrants consisted of the following:

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

The fair value of the warrants was estimated to be $216,000 and $518,000 as of December 31, 2011 and 2012, respectively. The key assumptions in the option-pricing valuation method as of December 31, 2011 and 2012 are as follows:

	December 31,	
	2011	2012
Value of Company equity	$ 23.5 million	$ 145.8 million
Expected volatility	80.0%	75.0%
Expected time to liquidity event	3.0 years	2.0 years
Risk-free interest rate	0.36%	0.25%

The Company recorded $13,000, $302,000 and $315,000 to other expense for the years ended December 31, 2011 and 2012 and for the period from April 22, 2010 (Inception) through December 31, 2012, respectively, representing the change in fair value of the warrants between the issuance date and the end of the reporting period.

10. Common Stock

The Company has reserved sufficient shares of common stock for issuance upon conversion of convertible preferred stock, exercise of stock options, and exercise of warrants. Common stockholders are entitled to dividends if and when declared by the Board of Directors subject to the prior rights of the preferred stockholders. As of December 31, 2012, no common stock dividends had been declared by the Board of Directors.

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

Notes to Financial Statements (continued)

10. Common Stock (continued)

The Company had reserved shares of common stock, on an as-converted basis, for future issuance as follows:

	December 31,	
	2011	2012
Convertible preferred stock	5,759,277	19,598,486
Convertible preferred stock warrants	327,853	353,459
2011 equity incentive plan	1,451,580	1,520,967
Shares available for future stock option grants	927,104	1,815,245
	8,465,814	23,288,157

11. Convertible Preferred Stock

Under the Company s Amended and Restated Certificate of Incorporation, as amended, the Company is authorized to issue two classes of shares: preferred and common stock. The preferred stock is issuable in series, and the Company s board of directors is authorized to determine the rights, preferences and terms of each series. As of December 31, 2011 and 2012, convertible preferred stock consisted of the following (in thousands, except share and per share amounts):

	As of December 31, 2011			
Convertible Preferred Stock:	**Shares Authorized**	**Shares Issued and Outstanding**	**Proceeds Net of Issuance Costs**	**Aggregate Liquidation Preference**
			(In thousands)	
Series A	62,000,000	18,052,464	$ 18,543	$ 19,272

	As of December 31, 2012			
Convertible Preferred Stock:	**Shares Authorized**	**Shares Issued and Outstanding**	**Proceeds Net of Issuance Costs**	**Aggregate Liquidation Preference**
			(In thousands)	
Series A	35,377,556	34,349,894	$ 33,623	$ 35,613
Series B	27,081,680	27,081,680	73,929	75,060
Total convertible preferred stock	62,459,236	61,431,574	$ 107,552	$ 110,673

The liquidation preference consists of the liquidation preference on the outstanding shares of the convertible preferred stock and the dividends in arrears on such shares in the amount of $607,000 and $159,000 as of December 31, 2011 and 2012.

Significant provisions of the convertible preferred stock are as follows:

Dividends When and as declared by the Company s Board of Directors, the holders of the Series A convertible preferred stock (Series A) and the Series B convertible preferred stock (Series B), collectively referred to as Preferred Stock, are entitled to receive dividends, out of any assets legally available therefor, prior and in preference to the declaration or payment of any dividend on the common stock or other securities and rights convertible of the Company, at the rate of $0.062 per share per annum, payable in the form of cash or property or, upon conversion of the preferred stock to common stock, payable in cash. Prior to the issuance of the Series B convertible preferred stock in December 2012, the Company was able to pay dividends in cash or additional shares of Series A convertible preferred stock. Such dividends shall accrue

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

Notes to Financial Statements (continued)

11. Convertible Preferred Stock (continued)

on each share from the date of issuance of such share, and shall accrue from day to day, whether or not earned or declared, and whether or not there are profits, surplus, shares, or other funds legally available for the payment of such dividends. Such dividends shall be cumulative so that, except as provided below, if such dividends in respect of any previous or current annual dividend period, at the annual rate specified above, shall not have been paid, the deficiency shall first be fully paid before any dividend or other distribution shall be paid on or declared and set apart for the common stock. Any accumulation of dividends on the Preferred Stock shall not bear interest. Cumulative dividends with respect to a share of Preferred Stock that are accrued, payable, and/or in arrears shall, upon conversion of such share to common stock, be paid to the extent assets are legally available therefor, and any amounts for which assets are not legally available shall be paid promptly as assets become legally available therefor. Any partial payment shall be made ratably among the holders of Preferred Stock in proportion to the payment each such holder would receive if the full amount of such dividends were paid. After dividends have been paid to the holders of the preferred stock, any additional dividends shall be paid among the holders of the preferred stock and common stock then outstanding in proportion to the greatest whole number of shares of common stock held (assuming conversion of Preferred Stock).

During 2012, $2,070,000 of preferred stock dividends were declared and paid to holders of Series A convertible preferred stock in the form of additional shares of Series A convertible preferred stock. Dividends in arrears as of December 31, 2011 and 2012 totaled $607,000 and $159,000, respectively, for both series of preferred stock.

Liquidation In the event of any liquidation, dissolution, or winding up of the Company, either voluntary or involuntary, the holders of Series A and Series B shall be entitled to receive, on a pari passu basis, prior and in preference to any distribution of any of the assets of this Corporation to the holders of common stock by reason of their ownership thereof, an amount per share equal to the sum of $1.034 (the Original Series A Issue Price) for each outstanding share of Series A convertible preferred stock (subject to adjustment for recapitalizations) and $2.769 (the Original Series B Issue Price) for each outstanding share of Series B convertible preferred stock (subject to adjustment for recapitalizations) and an amount equal to all declared or accrued but unpaid dividends on such shares. If available assets are insufficient to pay the full liquidation preference, the available assets will be distributed ratably among the holders of preferred stock. If there are excess assets to be allocated upon liquidation beyond what is described above, holders of preferred stock and common stock will share in such assets on an as-converted basis. However, the holders of Series A shall not be entitled to further participate in any distribution of the remaining assets of the corporation following the receipt of aggregate distributions equal to $3.102, plus any declared or accrued but unpaid dividends, and the holders of Series B shall not be entitled to further participate in any distribution of the remaining assets of the corporation following the receipt of aggregate distributions equal to $8.308, plus any declared or accrued but unpaid dividends.

Redemption At any time after June 16, 2017, but within 60 days after the receipt by this Corporation of a written request from the holders of not less than 75% of the then outstanding shares of Series A convertible preferred stock that all shares of Series A be redeemed, the Company shall, to the extent it may lawfully do so, redeem (the payment date being referred to herein as a Series A Redemption Date) all of the then-outstanding shares of Series A by paying in cash in exchange for the shares of Series A to be redeemed a sum equal to the greater of (i) the original Series A issue price per share of Series A (subject to adjustment for any recapitalizations) plus all declared or accrued but unpaid dividends on such shares and (ii) the then-current fair market value per share of Series A plus all declared or accrued but unpaid dividends on such shares (but only if, and to the extent, such dividends are not reflected in the fair market value) as determined

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

Notes to Financial Statements (continued)

11. Convertible Preferred Stock (continued)

in good faith by the Board of Directors of the Company, and taking into account any independent third-party valuation reasonably requested by the holders of at least 75% of the Series A then outstanding; however, any holder of Series A may elect, by delivery of notice to the Company at least five days prior to the Series A redemption date, not to have such holder s shares of Series A preferred stock redeemed. As only the passage of time is required for Series A to become redeemable, the Company is accreting the carrying value of Series A to its redemption value over the period from the date of issuance to June 16, 2017 (the earliest redemption date) using the interest method.

The Series B convertible preferred stock is not redeemable.

Voting Each holder of shares of preferred stock shall be entitled to the number of votes equal to the number of shares of common stock into which such shares of Preferred Stock could be converted and shall have voting rights and powers equal to the voting rights and powers of the common stock, and shall vote together with the common stock as a single class on an as-converted basis on all matters as to which holders of common stock have the right to vote. So long as at least 3,000,000 shares of Series A remain outstanding, the holders of Series A will be allowed to elect three directors of the Company, the holders of the common stock will be allowed to elect two directors of the Company, and any remaining directors will be elected by the holders of preferred stock and common stock, voting together as a single class.

Conversion Each share of preferred stock, at the option of the holder, is convertible into common stock determined by dividing the Original Series A issue price or Original Series B issue price, as applicable, by the conversion price applicable to such share in effect on the date the certificate is surrendered for conversion, subject to certain provisions for adjustment of the conversion price. Conversion of each share of preferred stock is automatic upon the closing of a firm commitment underwritten public offering with aggregate proceeds of not less than $30.0 million (before deduction of underwriting discounts and commissions) or the agreement or written consent of holders of at least seventy-five percent (75%) of the then-outstanding shares of preferred stock. As of December 31, 2012, all shares of preferred stock are convertible into common stock on a 3.1345-for-one basis.

12. Stock-Based Awards
2011 Equity Incentive Plan

In 2011, the Company adopted the 2011 Equity Incentive Plan (the Plan). The Plan provides for the granting of stock-based awards to employees, directors, and consultants under terms and provisions established by the Board of Directors. Under the terms of the Plan, options may be granted at an exercise price not less than fair market value. For employees holding more than 10% of the voting rights of all classes of stock, the exercise prices for incentive and nonstatutory stock options must be at least 110% of fair market of the common stock on the grant date, as determined by the Board of Directors. The terms of options granted under the Plan may not exceed ten years.

Options granted generally vest over a period of four years. Typically, the vesting schedule for option grants to newly hired employees provides that 1/4 of the grant vests upon the first anniversary of the employee s date of hire, with the remainder of the shares vesting monthly thereafter at a rate of 1/48 of the total shares subject to the option. All other options typically vest in equal monthly installments over the four-year vesting schedule.

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

Notes to Financial Statements (continued)

12. Stock-Based Awards (continued)

A summary of activity under the 2011 Plan and related information are as follows:

		Options Outstanding			
	Shares Available for Grant	Number of Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value (In thousands)
Outstanding December 31, 2010					
Shares reserved	2,378,684				
Options granted	(1,451,580)	1,451,580	$ 0.31		
Outstanding December 31, 2011	927,104	1,451,580	0.31	9.88	
Shares reserved	1,377,836				
Options granted	(499,278)	499,278	0.81		
Options exercised		(420,308)	0.31		
Options cancelled	9,583	(9,583)	0.31		
Outstanding December 31, 2012	1,815,245	1,520,967	$ 0.47	9.11	$ 2,038
Vested and exercisable December 31, 2012		99,233	$ 0.31	8.88	$ 149
Vested and expected to vest December 31, 2012		1,478,327	$ 0.47	9.11	$ 1,981

The aggregate intrinsic values of options outstanding, vested and exercisable, and vested and expected to vest were calculated as the difference between the exercise price of the options and the estimated fair value of the Company s common stock as determined by the Company s Board of Directors as of December 31, 2012. The total intrinsic value of options exercised during the years ended December 31, 2011 and 2012 and for the period from April 22, 2010 (Inception) through December 31, 2012 was $0, $211,000 and $211,000, respectively.

The options outstanding and exercisable by exercise price as of December 31, 2012, are as follows:

	Options Outstanding			Options Exercisable	
Exercise Price	Number Outstanding	Weighted-Average Remaining Contractual Life (in Years)	Number Exercisable	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Life (in Years)
$0.31	1,021,689	8.88	99,233	$ 0.31	8.88

$0.81	499,278	9.60				
	1,520,967	9.11	99,233	$	0.31	8.88

The weighted-average estimated fair value of stock options granted was $0.34, $0.47 and $0.38 per share of the Company s common stock during the years ended December 31, 2011 and 2012 and for the period from April 22, 2010 (Inception) through December 31, 2012, respectively. No options were granted in 2010.

The total estimated fair value of options vested during the years ended December 31, 2011 and 2012 and for the period from April 22, 2010 (Inception) through December 31, 2012 was $6,000, $172,000 and $178,000, respectively.

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

Notes to Financial Statements (continued)

12. Stock-Based Awards (continued)

Founder s Stock

In connection with the Series A preferred stock financing, the Company entered into a stock repurchase agreement with the founder on June 16, 2011, where the 2,552,241 common shares previously owned by the founder are now subject to repurchase by the Company at the original issuance price in the event that the founder s employment is terminated either voluntarily or involuntarily. Such repurchase rights lapse over a period of two years from June 16, 2011. The Company calculated the fair value of these restricted shares at the time the restriction was added to the shares as $1,199,000 and is recording this amount as stock-based compensation ratably as the repurchase rights lapse. Stock-based compensation expense pertaining to the founder s stock was $218,000, $713,000 and $931,000 during the years ended December 31, 2011 and 2012 and for the period from April 22, 2010 (Inception) through December 31, 2012, respectively. As of December 31, 2012, 638,060 of these shares remained subject to repurchase and $268,000 of stock compensation remained unamortized.

Stock-Based Compensation Expense

Total stock-based compensation recognized was as follows (in thousands):

	Year Ended December 31,		Period from April 22, 2010 (Inception) through December 31, 2012
	2011	2012	
Research and development	$ 28	$ 130	$ 158
General and administrative	226	761	987
Total stock-based compensation expense	$ 254	$ 891	$ 1,145

As of December 31, 2012, the total unrecognized compensation expense related to unvested options, net of estimated forfeitures, was $495,000, which the Company expects to recognize over an estimated weighted average period of 2.8 years.

In determining the fair value of the stock-based awards, the Company uses the Black-Scholes option-pricing model and assumptions discussed below. Each of these inputs is subjective and generally requires significant judgment to determine.

Expected Term The Company s expected term represents the period that the Company s stock-based awards are expected to be outstanding and is determined using the simplified method (based on the mid-point between the vesting date and the end of the contractual term).

Expected Volatility Since the Company is privately held and does not have any trading history for its common stock, the expected volatility was estimated based on the average volatility for comparable publicly traded biopharmaceutical companies over a period equal to the expected term of the stock option grants. When selecting comparable publicly traded biopharmaceutical companies on which it has based its expected stock price volatility, the Company selected companies with comparable characteristics to it, including enterprise value, risk profiles, position within the industry, and with historical share price information sufficient to meet the expected life of the stock-based awards. The historical volatility data was computed using the daily closing prices for the selected companies shares during the equivalent period of the calculated expected term of the stock-based awards. The Company will continue to apply this process until a sufficient amount of historical information regarding the volatility of its own stock price becomes available.

Risk-Free Interest Rate The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of option.

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ULTRAGENYX PHARMACEUTICAL INC.

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Notes to Financial Statements (continued)

12. Stock-Based Awards (continued)

Expected Dividend The Company has never paid dividends on its common stock and has no plans to pay dividends on its common stock. Therefore, the Company used an expected dividend yield of zero.

The fair value of stock option awards was estimated at the date of grant using a Black-Scholes option-pricing model with the following weighted average assumptions:

	Year Ended December 31,		Period from April 22, 2010 (Inception) through December 31, 2012
	2011	2012	
Expected term	6.25 years	6.25 years	6.25 years
Expected volatility	75%	67%	73%
Risk-free interest rate	1.15%	0.62%	1.01%
Dividend yield			

13. Income Taxes

The Company did not record a provision or benefit for income taxes during the years ended December 31, 2011 and 2012. The Company has incurred net operating losses since inception. The Company has not reflected any benefit of such net operating loss carryforwards in the accompanying financial statements. The Company has established a full valuation allowance against its deferred tax assets due to the uncertainty surrounding the realization of such assets.

The effective tax rate of our provision for income taxes differs from the federal statutory rate as follows:

	Year Ended December 31,	
	2011	2012
Federal statutory income tax rate	34.0%	34.0%
State income taxes, net of federal benefit	5.3	6.0
Federal tax credits	5.5	8.6
Nondeductible permanent items	(1.5)	
Stock compensation	(1.3)	(1.9)
Change in valuation allowance	(32.9)	(46.0)
Adjustment of loss carryforwards	(9.0)	
Other	(0.1)	(0.7)
	0.0%	0.0%

The tax effect of temporary differences that give rise to significant portions of the deferred tax assets is presented below (in thousands):

	December 31, 2011	December 31, 2012
Deferred tax assets:		
Net operating loss carryforwards	$ 1,812	$ 6,186
Tax credits	756	3,619
Other	(18)	272
Total deferred tax assets	2,550	10,077
Valuation allowance	(2,550)	(10,077)
Net deferred tax assets	$	$

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ULTRAGENYX PHARMACEUTICAL INC.

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Notes to Financial Statements (continued)

13. Income Taxes (continued)

Additionally, the future utilization of the net operating loss carryforwards to offset future taxable income may be subject to an annual limitation, pursuant to Internal Revenue Code Section 382, as a result of ownership changes that may have occurred previously or that could occur in the future. A Section 382 analysis to determine the limitation of the net operating loss carryforwards has not been performed. Until this analysis has been performed, the deferred tax assets for net operating losses of $725,000 generated through December 31, 2012, have been removed from the deferred tax asset schedule and a corresponding decrease to the valuation allowance has been recorded. This represents the amount estimated to expire before utilization, assuming a change in ownership has occurred. The Company recorded unrecognized tax benefits for uncertainty in income taxes. Due to the existence of the valuation allowance, future changes in unrecognized tax benefits will not impact the effective tax rate. The valuation allowance increased by $7.5 million and $10.1 million during the year ended December 31, 2012 and for the period from April 22, 2010 (Inception) through December 31, 2012.

As of December 31, 2012, the Company had approximately $14.9 million and $19.3 million of federal and state NOL carryforwards available to reduce future taxable income that will begin to expire in 2030 for federal and 2030 for state tax purposes.

As of December 31, 2012, the Company also had research and development tax credit carryforwards of approximately $152,000 and $296,000 for federal and state purposes available to offset future regular and alternative minimum taxable income. If not utilized, the federal carryforwards will expire in various amounts beginning in 2030, and the state credits can be carried forward indefinitely.

On January 2, 2013, the American Taxpayer Relief Act of 2012 (the Act) was passed in to law. The Act included a retroactive extension of the U.S. research credit for 2012. Since the effects of the tax law changes are recognized in the first period the Company would recognize $109,000 of additional research credits as a discrete item during the first quarter of 2013. The tax effects of the research credits will be offset by valuation allowance and will not impact the financial statements.

As of December 31, 2012, the Company had an Orphan Drug Credit of approximately $4.8 million for federal tax purposes available to offset future regular and alternative minimum taxable income.

Uncertain Tax Positions

A reconciliation of the Company s unrecognized tax benefits for the years ended December 31, 2011 and 2012 is as follows (in thousands):

	December 31,	
	2011	**2012**
Balance at beginning of year	$	$ 324
Additions based on tax positions related to current year	324	1,227
Additions (reductions) for tax positions of prior years		
Balance at end of year	$ 324	$ 1,551

The entire amount of the unrecognized tax benefits would not impact the Company s effective tax rate if recognized. The Company has elected to include interest and penalties as a component of tax expense. During the years ended December 31, 2011 and 2012, the Company did not recognize accrued interest and penalties related to unrecognized tax benefits. The Company does not anticipate that the amount of existing unrecognized tax benefits will significantly increase or decrease during the next 12 months.

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

Notes to Financial Statements (continued)

13. Income Taxes (continued)

The Company files income tax returns in the U.S. federal jurisdiction and California tax jurisdictions. The federal and state income tax returns from inception to December 31, 2012 remain subject to examination.

14. Net Loss and Pro Forma 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 during the years ended December 31, 2011 and 2012 (in thousands, except share and per share data):

	Year Ended December 31,	
	2011	2012
Numerator:		
Net loss	$ (6,849)	$ (16,334)
Accretion and dividends on convertible preferred stock	(617)	(3,227)
Net loss attributable to common stockholders	$ (7,466)	$ (19,561)
Denominator:		
Weighted-average common shares outstanding	3,008,880	3,118,798
Less: weighted-average unvested common shares subject to repurchase	(1,391,496)	(1,741,591)
Weighted-average shares used to compute net loss per share attributable to common stockholders, basic and diluted	1,617,384	1,377,207
Net loss per share attributable to common stockholders, basic and diluted	$ (4.62)	$ (14.20)

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:

	December 31,	
	2011	2012
Convertible preferred stock	3,124,211	8,354,772
Stock options to purchase common stock	177,503	1,563,217
Common stock subject to repurchase	1,391,496	1,741,590
Convertible preferred stock warrants	294,120	353,459
	4,987,330	12,013,038

Unaudited Pro Forma

A dividend of $4.3 million is payable concurrent with the conversion of the Company s preferred stock, which has been calculated as if the conversion of preferred stock into common stock occurred as of January 30, 2014, and will be paid from the proceeds of an initial public offering as the Company incurred a net loss for the year ended December 31, 2012. As a result, the pro forma net loss per share attributable to common stockholders, basic and diluted, for the year ended December 31, 2012 gives effect to the number of shares that would be required to be issued at an initial public offering price of $21.00 per share to pay the amount of dividends. The number of shares used in computing the Company s unaudited pro forma basic and diluted net loss per share attributable to common stockholders includes the assumed issuance of 203,857 shares of common stock. In addition, the calculation of the pro forma net loss per share attributable to common stockholders, basic and diluted, assumes the conversion of all outstanding shares of preferred stock into shares of common stock.

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

Notes to Financial Statements (continued)

14. Net Loss and Pro Forma Net Loss per Share Attributable to Common Stockholders (continued)

The following table sets forth the computation of the Company s unaudited pro forma basic and diluted net loss per share attributable to common stockholders during the year ended December 31, 2012 (in thousands, except for share and per share amounts):

	Year Ended December 31, 2012
Net loss	$ (16,334)
Dividends to be paid on convertible preferred stock	(4,281)
Change in fair value of convertible preferred stock warrant liabilities	302
Net loss used in computing pro forma net loss per share attributable to common stockholders, basic and diluted	$ (20,313)
Shares used in computing net loss per share attributable to common stockholders, basic and diluted	1,377,207
Shares required to be issued to pay the dividends payable	203,857
Pro forma adjustments to reflect assumed conversion of convertible preferred stock	8,354,772
Shares used in computing pro forma net loss per share attributable to common stockholders, basic and diluted	9,935,836
Pro forma net loss per share attributable to common stockholders, basic and diluted	$ (2.04)

15. Subsequent Events

On June 26, 2013, the Company notified BRI that it was exercising its option to license the rights to triheptanoin in all territories outside of the United States, Canada and Mexico. The option exercise fee associated with this is $750,000.

On August 29, 2013, the Company entered into a collaboration and license agreement with Kyowa Hakko Kirin Co. LTD. (KHK). Under the terms of this collaboration and license agreement, the Company and KHK will collaborate on the development and commercialization of certain products containing KRN23, an antibody directed towards FGF23, in the field of orphan diseases in the United States and Canada, or the profit share territory, and in the European Union, Switzerland, and Turkey, or the European territory, and the Company will have the right to develop and commercialize such products in the field of orphan diseases in Mexico and Central and South America, or Latin America. In the field of orphan diseases, and except for ongoing studies being conducted by KHK, the Company will be the lead party for development activities in the profit share territory and in the European territory until the applicable transition date. The Company will share the costs for development activities in the profit share territory and European territory conducted pursuant to the development plan before the applicable transition date equally with KHK. On the applicable transition date in the relevant territory, KHK will become the lead party and be responsible for these costs. However, the Company will continue to share the costs of the studies commenced prior to the applicable transition date equally with KHK. The Company has the primary responsibility for conducting certain research and development services. The Company is obligated to provide assistance in accordance with the agreed upon development plan as well as participate on various committees. If KRN23 is approved, the Company and KHK will share commercial responsibilities and profits in the profit share territory until the applicable transition date, KHK will commercialize KRN23 in the European territory and the Company will develop and commercialize KRN23 in Latin America. KHK will manufacture and supply KRN23 for clinical use globally and will manufacture and supply KRN23 for commercial use in the profit share territory and Latin America.

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

CONDENSED BALANCE SHEETS

(In thousands, except share and per share amounts)

	December 31, 2012 (Note 1)	September 30, 2013 (Unaudited)	Pro Forma Stockholders Equity as of September 30, 2013 (Unaudited)
Assets			
Current assets:			
Cash and cash equivalents	$ 86,190	$ 6,049	
Short term investments		57,608	
Accounts receivable		38	
Prepaid expenses and other current assets	255	2,980	
Total current assets	86,445	66,675	
Property and equipment, net	1,362	1,308	
Restricted cash	476	451	
Other assets	33	158	
TOTAL ASSETS	$ 88,316	$ 68,592	
Liabilities, Convertible Preferred Stock and Stockholders (Deficit) Equity			
Current liabilities:			
Accounts payable	$ 1,200	$ 2,890	
Accrued liabilities	1,913	2,643	$ 6,924
Deferred rent current portion	75	75	
Total current liabilities	3,188	5,608	
Convertible preferred stock warrant liability	518	1,596	
Other liabilities	270	234	
Total liabilities	3,976	7,438	
Commitments and contingencies			
Series A redeemable convertible preferred stock, par value of $0.001 per share 35,377,556 shares authorized as of December 31, 2012 and September 30, 2013 (unaudited); 34,349,894 shares issued and outstanding as of December 31, 2012 and September 30, 2013 (unaudited), no shares authorized, issued and outstanding, pro forma (unaudited); redemption value of $90,704 of September 30, 2013 (unaudited)	37,458	44,073	
Series B convertible preferred stock, par value of $0.001 per share 27,081,680 shares authorized as of December 31, 2012 and September 30, 2013 (unaudited); 27,081,680 shares issued and outstanding as of December 31, 2012 and September 30, 2013 (unaudited), no shares authorized, issued and outstanding, pro forma (unaudited); aggregate liquidation preference of	73,929	73,929	

$76,316 as of September 30, 2013 (unaudited)			
Stockholders (deficit) equity:			
Common stock, par value of $0.001 per share 85,000,000 shares authorized as of December 31, 2012 and September 30, 2013 (unaudited); 3,458,928 and 3,703,016 shares issued and outstanding as of December 31, 2012 and September 30, 2013 (unaudited), 250,000,000 shares authorized, 23,301,502 shares issued and outstanding, pro forma (unaudited)	3	4	23
Additional paid-in capital	8	8	115,306
Accumulated other comprehensive loss		(14)	(14)
Deficit accumulated during the development stage	(27,058)	(56,846)	(56,846)
Total stockholders (deficit) equity	(27,047)	(56,848)	$ 58,469
Total liabilities, convertible preferred stock and stockholders (deficit) equity	$ 88,316	$ 68,592	

See accompanying notes.

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

CONDENSED STATEMENTS OF OPERATIONS

(Unaudited)

(In thousands, except share and per share amounts)

	Nine Months Ended September 30,		Period from April 22, 2010 (Inception) Through September 30,
	2012	2013	2013
Operating expenses:			
Research and development	$ 8,866	$ 19,625	$ 37,941
General and administrative	2,441	3,130	8,610
Total operating expenses	11,307	22,755	46,551
Loss from operations	(11,307)	(22,755)	(46,551)
Other income (expense), net:			
Interest income		157	162
Interest expense			(318)
Other expense	(97)	(1,155)	(1,535)
Total other income (expense), net	(97)	(998)	(1,691)
Net loss	$ (11,404)	$ (23,753)	$ (48,242)
Net loss attributable to common stockholders	$ (12,749)	$ (31,624)	
Net loss per share attributable to common stockholders, basic and diluted	$ (12.35)	$ (9.70)	
Shares used in computing net loss per share attributable to common stockholders, basic and diluted	1,032,159	3,260,484	
Pro forma net loss per share attributable to common stockholders, basic and diluted		$ (1.17)	
Shares used in computing pro forma net loss per share attributable to common stockholders, basic and diluted		23,062,827	

See accompanying notes.

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

CONDENSED STATEMENTS OF COMPREHENSIVE LOSS

(Unaudited)

(In thousands)

	Nine Months Ended September 30,		Period from April 22, 2010 (Inception) Through September 30, 2013
	2012	2013	
Net loss	$ (11,404)	$ (23,753)	$ (48,242)
Other comprehensive loss:			
Unrealized loss on available-for-sale securities		(14)	(14)
Total comprehensive loss	$ (11,404)	$ (23,767)	$ (48,256)

See accompanying notes.

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

CONDENSED STATEMENTS OF CASH FLOWS

(Unaudited)

(In thousands)

	Nine Months Ended September 30,		Period from April 22, 2010 (Inception) Through September 30, 2013
	2012	2013	
Cash flows from operating activities:			
Net loss	$ (11,404)	$ (23,753)	$ (48,242)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	221	332	685
Amortization of premium on securities		972	972
Noncash interest expense			318
Stock-based compensation	694	447	1,592
Revaluation of preferred stock warrant liability	67	1,078	1,393
Changes in operating assets and liabilities:			
Accounts receivable		(38)	(38)
Prepaid expenses and other current assets	(10)	(2,725)	(2,980)
Other assets	5	(125)	(158)
Accounts payable	817	1,690	2,890
Accrued expenses and other liabilities	820	695	2,952
Net cash used in operating activities	(8,790)	(21,427)	(40,616)
Cash flows from investing activities:			
Purchase of property and equipment	(967)	(278)	(1,993)
Decrease (increase) in restricted cash	(100)	25	(451)
Purchase of investments		(63,056)	(63,056)
Proceeds from maturities of investments		4,462	4,462
Net cash used in investing activities	(1,067)	(58,847)	(61,038)
Cash flows from financing activities:			
Net proceeds from issuance of convertible preferred stock, net of issuance costs	15,080		103,888
Net proceeds from issuance of common stock	48	133	265
Proceeds from issuance of promissory notes	100		3,550
Net cash provided by financing activities	15,228	133	107,703
Net increase (decrease) in cash and cash equivalents	5,371	(80,141)	6,049
Cash and cash equivalents Beginning of period	10,645	86,190	
Cash and cash equivalents End of period	$ 16,016	$ 6,049	$ 6,049

See accompanying notes.

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

Notes to Unaudited Interim Condensed Financial Statements

1. Summary of Significant Accounting Policies
Unaudited Interim Condensed Financial Statements

The interim condensed balance sheet as of September 30, 2013 and the statements of operations, comprehensive loss and cash flows for the nine months ended September 30, 2012 and 2013 are unaudited. The unaudited interim financial statements have been prepared on the same basis as the annual financial statements and, in the opinion of management, reflect all adjustments, which include only normal recurring adjustments, necessary to present fairly the Company s financial position as of September 30, 2013 and its results of operations and cash flows for the nine months ended September 30, 2012 and 2013. The financial data and the other financial information disclosed in these notes to financial statements related to the nine month periods are also unaudited. The results of operations for the nine months ended September 30, 2013 are not necessarily indicative of the results to be expected for the year ending December 31, 2013 or for any other future annual or interim period. The condensed balance sheet as of December 31, 2012 included herein was derived from the audited financial statements as of that date. These financial statements should be read in conjunction with the Company s audited financial statements included elsewhere in this prospectus.

Unaudited Pro Forma Stockholders Equity

The pro forma stockholders equity as of September 30, 2013 presents the Company s stockholders equity as though all of the Company s outstanding convertible preferred stock had automatically converted into shares of common stock upon the completion of an initial public offering (IPO) of the Company s common stock. In addition, the pro forma stockholders equity assumes the reclassification of the convertible preferred stock warrant liability to additional paid-in capital upon completion of an IPO of the Company s common stock, as the warrants upon an IPO become common stock warrants that are not subject to remeasurement. The pro forma stockholders equity also assumes the payment in cash of a dividend on the convertible preferred stock which is triggered upon the conversion of the convertible preferred stock to common stock. For the purpose of this pro forma presentation, the dividend payable has been calculated as if the conversion occurred as of January 30, 2014, the date of this filing.

Use of Estimates

The accompanying financial statements have been prepared in accordance with U.S. generally accepted accounting principles (GAAP). The preparation of the financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, disclosure of contingent assets and liabilities and the reported amounts of expenses in the financial statements and the accompanying notes. On an ongoing basis, management evaluates its estimates, including those related to clinical trial accruals, fair value of assets and liabilities, convertible preferred stock and related warrants, common stock, income taxes and stock-based compensation. Management bases its estimates on historical experience and on various other market-specific and relevant assumptions that management believes to be reasonable under the circumstances. Actual results could differ from those estimates.

Additional Capital Requirements

The Company has incurred significant losses and negative cash flows from operations. At September 30, 2013, the Company had a total deficit accumulated during the development stage of $56.8 million and cash, cash equivalents and marketable securities of $63.7 million. Management believes that currently available resources

will provide sufficient funds to enable the Company to meet its obligations through at least December 31, 2013.

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

Notes to Unaudited Interim Condensed Financial Statements (continued)

1. Summary of Significant Accounting Policies (continued)

However, if the Company s anticipated operating results are not achieved in future periods, planned expenditures may need to be reduced in order to extend the time period over which the then-available resources would be able to fund its operations. The Company will need to raise additional capital to fully implement its business plan.

Cash and Cash Equivalents

The Company considers all highly liquid investments with original maturities of three months or less at the time of purchase to be cash equivalents. Cash equivalents consist primarily of money market funds and are stated at fair value.

Marketable Securities

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

Concentration of Credit Risk and Other Risks and Uncertainties

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

Deferred Offering Costs

Deferred offering costs, which primarily consist of direct incremental legal and accounting fees relating to the IPO, are capitalized. The deferred offering costs will be offset against IPO proceeds upon the consummation of the offering. In the event the offering is terminated, deferred offering costs will be expensed. As of September 30, 2013, $1.4 million of deferred offering costs were capitalized in prepaid and other current assets on the balance sheet. There were no such costs capitalized as of December 31, 2012.

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

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

Notes to Unaudited Interim Condensed Financial Statements (continued)

1. Summary of Significant Accounting Policies (continued)

during the period without consideration of 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 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.

Unaudited Pro Forma Net Loss per Share Attributable to Common Stockholders

Pro forma basic and diluted net loss per share attributable to common stockholders has been computed to give effect to the conversion of the convertible preferred stock into common stock. Also, the numerator in the pro forma basic and diluted net loss per share attributable to common stockholders calculation has been adjusted to remove gains and losses resulting from remeasurement of the convertible preferred stock warrant liability as these amounts will be reclassified to additional paid-in capital upon a qualifying initial public offering of the Company s common stock, and has also been adjusted to reflect the payment of a dividend to the holders of the Company s preferred stock concurrent with the conversion of the Company s convertible preferred stock to common stock immediately prior to the completion of this offering. The denominator in the pro forma basic and diluted net loss per share attributable to common stockholders has been adjusted to give effect to the number of shares that would be required to be issued at an initial public offering price of $21.00 per share to pay the $4.3 million dividend to the convertible preferred stockholders. The pro forma net loss per share attributable to common stockholders does not include the shares expected to be sold and related proceeds to be received from an initial public offering.

Recently Issued Accounting Pronouncements

In February 2013, the Financial Accounting Standards Board (FASB) issued Accounting Standards Update (ASU) No. 2013-02, *Other Comprehensive Income (Topic 220): Reporting of Amounts Reclassified Out of Accumulated Other Comprehensive Income*. ASU No. 2013-02 supersedes the presentation requirements for reclassifications out of accumulated other comprehensive income in ASU 2011-05 and 2011-12 and requires an entity to provide additional information about reclassifications out of accumulated other comprehensive income. The Company adopted this guidance on January 1, 2013 on a prospective basis. The adoption of this amendment did not have a material impact on the Company s results of operations or financial position.

Reverse Stock Split

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

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

Notes to Unaudited Interim Condensed Financial Statements (continued)

2. Fair Value Measurements

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

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

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

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

The Company s financial instruments consist of Level 1 and 2 assets and Level 3 liabilities. Where quoted prices are available in an active market, securities are classified as Level 1. Level 1 assets consist primarily of highly liquid money market funds that are included in cash and cash equivalents and restricted cash. The Company s Level 2 investments include corporate bonds. Level 2 inputs are based upon quoted prices for similar instruments in active markets, quoted prices for identical or similar instruments in markets that are not active and model-based valuation techniques for which all significant inputs are observable in the market or can be corroborated by observable market data for substantially the full term of the assets. Where applicable, these models project future cash flows and discount the future amounts to a present value using market-based observable inputs obtained from various third-party data providers, including but not limited to, benchmark yields, interest rate curves, reported trades, broker/dealer quotes and market reference data. Level 3 liabilities consist of the convertible preferred stock warrant liability. The determination of the fair value of the convertible preferred stock warrants is discussed in Note 4. Generally, increases or decreases in the fair value of the underlying convertible preferred stock would result in a directionally similar impact in the fair value measurement of the warrant liability.

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

Notes to Unaudited Interim Condensed Financial Statements (continued)

2. Fair Value Measurements (continued)

The following table sets forth the fair value of the Company s financial assets and liabilities measured at fair value on a recurring basis based on the three-tier fair value hierarchy (in thousands):

	December 31, 2012			
	Level 1	Level 2	Level 3	Total
Financial Assets:				
Money market funds	$ 376	$	$	$ 376
Total financial assets	$ 376	$	$	$ 376
Financial Liabilities:				
Convertible preferred stock warrant liability	$	$	$ 518	$ 518
Total financial liabilities	$	$	$ 518	$ 518

	September 30, 2013			
	Level 1	Level 2	Level 3	Total
Financial Assets:				
Money market funds	$ 4,835	$	$	$ 4,835
Commercial paper		999		999
Corporate bonds		56,765		56,765
Total financial assets	$ 4,835	$ 57,764	$	$ 62,599
Financial Liabilities:				
Convertible preferred stock warrant liability	$	$	$ 1,596	$ 1,596
Total financial liabilities	$	$	$ 1,596	$ 1,596

The following table sets forth a summary of the changes in the fair value of the Company s Level 3 financial liabilities (in thousands):

Balance as of December 31, 2012	$ 518
Change in fair value recorded in other expense	1,078
Balance as of September 30, 2013	$ 1,596

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

Notes to Unaudited Interim Condensed Financial Statements (continued)

3. Balance Sheet Components

Cash Equivalents, Restricted Cash and Marketable Securities

The fair values of cash equivalents, restricted cash and marketable securities classified as available-for-sale securities, consisted of the following:

	December 31, 2012			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Money market funds	$ 376	$	$	$ 376
Total	$ 376	$	$	$ 376

	September 30, 2013			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Money market funds	$ 4,835	$	$	$ 4,835
Commercial paper	999			999
Corporate bonds	56,779	7	(21)	56,765
Total	$ 62,613	$ 7	$ (21)	$ 62,599

The available-for-sale securities held as of September 30, 2013 had contractual maturities of less than two years.

Property and Equipment, net

Property and equipment, net consists of the following (in thousands):

	December 31, 2012	September 30, 2013
Research and development equipment	$ 225	$ 264
Office furniture and equipment	266	289
Computer equipment	187	235
Software	34	58
Leasehold improvements	1,003	1,147
Property and equipment, gross	1,715	1,993
Less accumulated depreciation and amortization	(353)	(685)
Property and equipment, net	$ 1,362	$ 1,308

Depreciation and amortization expense for the nine months ended September 30, 2012 and 2013 and the period from April 22, 2010 (Inception) through September 30, 2013 was $221,000, $332,000 and $685,000, respectively.

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

Notes to Unaudited Interim Condensed Financial Statements (continued)

3. Balance Sheet Components (continued)

Accrued Liabilities

Accrued liabilities consist of the following (in thousands):

	December 31, 2012	September 30, 2013
Research and clinical trial expenses	$ 595	$ 733
Payroll and related expenses	1,302	1,370
Accrued professional services		440
Other	16	100
Total accrued liabilities	$ 1,913	$ 2,643

4. Convertible Preferred Stock Warrants

As of December 31, 2012 and September 30, 2013, outstanding warrants consisted of the following:

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

The fair value of the warrants was estimated to be $518,000 and $1.6 million as of December 31, 2012 and September 30, 2013, respectively. The key assumptions in the option-pricing valuation method as of December 31, 2012 and September 30, 2013 are summarized in the table below.

	December 31, 2012	September 30, 2013
Value of Company equity	$145.8 million	$240.3 million
Expected volatility	75.0%	75.0%
Expected time to liquidity event	2.0 years	0.5 1.5 years

Risk-free interest rate	0.25%	0.04	0.22%

The Company recorded $67,000, $1.1 million and $1.4 million to other expense for the nine months ended September 30, 2012 and 2013 and for the period from April 22, 2010 (Inception) through September 30, 2013, respectively, representing the change in fair value of the warrants between the issuance date and the end of the reporting period.

5. Convertible Preferred Stock

The holders of the Series A and Series B convertible preferred stock are entitled to receive dividends at the rate of $0.062 per share per annum, payable in the form of cash. Dividends accrue from day to day, whether or not declared, but will be paid only when, as, and if declared by the Board of Directors. After dividends have been paid to the holders of the preferred stock, any additional dividends shall be paid among the holders of the preferred stock and common stock then outstanding in proportion to the greatest whole number of shares of common stock held (assuming conversion of Preferred Stock). During 2012, $2.1 million of dividends were declared and paid to holders of Series A convertible preferred stock in the form of additional Series A convertible preferred stock. Dividends in arrears as of December 31, 2012 and September 30, 2013, totaled $159,000 and $3.0 million, respectively, for both series of preferred stock.

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

Notes to Unaudited Interim Condensed Financial Statements (continued)

5. Convertible Preferred Stock (continued)

The Company initially recorded the Series A and Series B convertible preferred stock at their issuance price, which represents the carrying value. The Series A convertible preferred stock is redeemable at any time after June 16, 2017 once a written request to redeem such stock is received by the Company from holders of not less than seventy-five percent of the then outstanding Series A convertible preferred stock. As only the passage of time is required for the Series A convertible preferred stock to become redeemable, the difference in the initial carrying value of the Series A convertible preferred stock and their total redemption value is being accreted from the issuance date through the first redemption date of June 16, 2017. The Company recorded accretion of $116,000 and $6.6 million for the nine months ended September 30, 2012 and 2013, respectively.

6. License Agreements
Baylor Research Institute

In September 2012, the Company entered into a license agreement with Baylor Research Institute (BRI). Under the terms of this license agreement, BRI exclusively licensed to the Company certain intellectual property related to triheptanoin for North America. Under the license agreement, the Company paid BRI an up-front fee of $250,000 which was recorded as research and development expense during the year ended December 31, 2012.

The Company has an exclusive option to expand the licensed territory to a worldwide license if the previous holder of such territorial rights allows that option to lapse. The previous holder s option lapsed on December 31, 2012, and on June 26, 2013, the Company notified BRI that it was exercising its exclusive option to expand the licensed territory. The fee associated with this option exercise was $750,000, which was recorded as research and development expense during the nine months ended September 30, 2013.

Kyowa Hakko Kirin Co. LTD.

On August 29, 2013, the Company entered into a collaboration and license agreement with Kyowa Hakko Kirin Co. Ltd. (KHK). Under the terms of this collaboration and license agreement, the Company and KHK will collaborate on the development and commercialization of certain products containing KRN23, an antibody directed towards FGF23, in the field of orphan diseases in the United States and Canada, or the profit share territory, and in the European Union, Switzerland, and Turkey, or the European territory, and the Company will have the right to develop and commercialize such products in the field of orphan diseases in Mexico and Central and South America, or Latin America. In the field of orphan diseases, and except for ongoing studies being conducted by KHK, the Company will be the lead party for development activities in the profit share territory and in the European territory until, with respect to the profit share territory, the fifth anniversary of the first commercial sale in the United States in the first indication and, with respect to the European territory, the date on which marketing approval for a licensed product for the first indication is obtained in the European territory on a country-by-country basis; each such date is referred to herein as the applicable transition date. The Company will share the costs for development activities in the profit share territory and European territory conducted pursuant to the development plan before the applicable transition date equally with KHK. On the applicable transition date in the relevant territory, KHK will become the lead party and be responsible for these costs. However, the Company will continue to share the costs of the studies commenced prior to the applicable transition date equally with KHK. The Company has the primary responsibility for conducting certain research and development services. The Company is obligated to provide assistance in accordance with the agreed upon development plan as well as participate on various committees. If KRN23 is approved, the Company and KHK will share commercial responsibilities and profits in the profit share territory until the applicable transition date, KHK will commercialize KRN23 in the European territory and the Company will develop and commercialize KRN23 in

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

Notes to Unaudited Interim Condensed Financial Statements (continued)

6. License Agreements (continued)

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 has incurred net development costs of $42,000 in connection with this agreement during the nine months ended September 30, 2013 and such costs have been recognized as research and development expenses.

7. Stock-Based Awards
2011 Equity Incentive Plan

The following table summarizes option activity under the 2011 Plan and related information during the nine months ended September 30, 2013:

	Shares Available for Grant	Options Outstanding	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value (in thousands)
Outstanding December 31, 2012	1,815,245	1,520,967	$ 0.47	9.11	
Options granted	(502,465)	502,465	2.07		
Options exercised		(244,088)	0.53		
Options cancelled	252,572	(252,572)	1.25		
Outstanding September 30, 2013	1,565,352	1,526,772	$ 0.86	8.65	$ 9,170
Vested and exercisable September 30, 2013		257,215	$ 0.41	8.26	$ 1,661
Vested and expected to vest September 30, 2013		1,488,701	$ 0.86	8.65	$ 8,945

The aggregate intrinsic values of options outstanding, vested and exercisable, and vested and expected to vest were calculated as the difference between the exercise price of the options and the estimated fair value of the Company s common stock as determined by the Company s Board of Directors as of September 30, 2013. The total intrinsic value of options exercised during the nine months ended September 30, 2012 and 2013 was $77,000 and $622,000, respectively.

The total estimated fair value of options vested during the nine months ended September 30, 2012 and 2013 was $83,000 and $158,000, respectively.

Founder s Stock

On June 16, 2011, 2,552,241 common shares were issued to the Company s founder, which are subject to repurchase by the Company at the original issuance price in the event that the founder s employment is terminated either voluntarily or involuntarily. Such repurchase rights lapse over a period of two years from June 16, 2011. The Company calculated the fair value of these restricted shares at the time the restriction was added to the shares as $1.2 million and was recording this amount as stock-based compensation ratably as the repurchase rights lapse. As of September 30, 2013, all of the founder s shares have vested and thus are no longer subject to repurchase.

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

Notes to Unaudited Interim Condensed Financial Statements (continued)

7. Stock-Based Awards (continued)

Stock Compensation Expense

Total stock-based compensation recognized for stock-based awards was as follows (in thousands):

	Nine Months Ended September 30,		Period from April 22, 2010 (Inception) through September 30, 2013
	2012	2013	
Research and development	$ 98	$ 139	$ 297
General and administrative	596	308	1,295
Total stock-based compensation expense	$ 694	$ 447	$ 1,592

As of September 30, 2013, there was $799,000 of total unrecognized compensation costs, net of estimated forfeitures, related to nonvested stock option awards that will be recognized on a straight-line basis over the weighted average remaining period of 2.4 years.

The weighted-average estimated fair value of stock options granted was $0.47 and $1.38 per share of the Company s common stock during the nine months ended September 30, 2012 and 2013, respectively. The estimated grant date fair value of the Company s equity-based awards issued to employees was calculated using the Black-Scholes option-pricing model, based on the following assumptions:

	Nine Months Ended September 30,	
	2012	2013
Expected term	6.25 years	6.25 years
Expected volatility	67%	75%
Risk-free interest rate	0.61%	0.92%
Dividend yield		

8. Net Loss and Pro Forma 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 during the nine months ended September 30, 2012 and 2013 (in thousands, except share and per share data):

	Nine Months Ended September 30,	
	2012	2013
Numerator:		

Net loss	$ (11,404)	$ (23,753)
Accretion and dividends on convertible preferred stock	(1,345)	(7,871)
Net loss attributable to common stockholders	$ (12,749)	$ (31,624)
Denominator:		
Weighted-average common shares outstanding	3,060,445	3,529,264
Less: weighted-average unvested common shares subject to repurchase	(2,028,286)	(268,780)
Weighted average shares used to compute net loss per share attributable to common stockholders, basic and diluted	1,032,159	3,260,484
Net loss per share attributable to common stockholders, basic and diluted	$ (12.35)	$ (9.70)

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

Notes to Unaudited Interim Condensed Financial Statements (continued)

8. Net Loss and Pro Forma Net Loss per Share Attributable to Common Stockholders (continued)

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:

	September 30,	
	2012	2013
Convertible preferred stock	9,794,521	19,598,486
Stock options to purchase common stock	1,523,513	1,599,858
Common stock subject to repurchase	2,028,286	268,780
Convertible preferred stock warrants	348,301	353,459
	13,694,621	21,820,583

Unaudited Pro Forma

A dividend of $4.3 million is payable concurrent with the conversion of the Company s preferred stock, which has been calculated as if the conversion of preferred stock into common stock occurred as of January 30, 2014, and will be paid from the proceeds of an initial public offering as the Company incurred a net loss for the nine months ended September 30, 2013. As a result, the pro forma net loss per share attributable to common stockholders, basic and diluted, for the nine months ended September 30, 2013 gives effect to the number of shares that would be required to be issued at an initial public offering price of $21.00 per share to pay the amount of dividends. The number of shares used in computing the Company s unaudited pro forma basic and diluted net loss per share attributable to common stockholders includes the assumed issuance of 203,857 shares of common stock. In addition, the calculation of the pro forma net loss per share attributable to common stockholders, basic and diluted, assumes the conversion of all outstanding shares of preferred stock into shares of common stock.

The following table sets forth the computation of the Company s unaudited pro forma basic and diluted net loss per share attributable to common stockholders during the nine months ended September 30, 2013 (in thousands, except for share and per share amounts):

	Nine Months Ended September 30, 2013
Net loss	$ (23,753)
Dividends to be paid on convertible preferred stock	(4,281)
Change in fair value of convertible preferred stock warrant liabilities	1,078
Net loss used in computing pro forma net loss per share attributable to common stockholders, basic and diluted	$ (26,956)
Shares used in computing net loss per share attributable to common stockholders, basic and diluted	3,260,484
Shares required to be issued to pay the dividends payable	203,857
Pro forma adjustments to reflect assumed conversion of convertible preferred stock	19,598,486

Shares used in computing pro forma net loss per share attributable to common stockholders, basic and diluted	23,062,827
Pro forma net loss per share attributable to common stockholders, basic and diluted	$ (1.17)

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ULTRAGENYX PHARMACEUTICAL INC.

(A Development Stage Company)

Notes to Unaudited Interim Condensed Financial Statements (continued)

9. Defined Contribution Plan

In March 2013, the Company began to sponsor a 401(k) retirement plan, in which substantially all of its full-time employees are eligible to participate. Participants may contribute a percentage of their annual compensation to this plan, subject to statutory limitations. The Company did not provide any contributions during the nine months ended September 30, 2013.

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5,760,369 shares

Common stock

Prospectus

J.P. Morgan **Morgan Stanley**

Cowen and Company

Canaccord Genuity

January 30, 2014

Until February 24, 2014, all dealers that buy, sell or trade in our common stock, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to the dealers obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.