Raptor Pharmaceutical Corp
Form 10-K
March 02, 2015

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d)
OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2014

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

Commission File Number: 000-25571

RAPTOR PHARMACEUTICAL CORP.
(Exact name of registrant as specified in its charter)

Delaware	86-0883978
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

7 Hamilton Landing, Suite 100, Novato, CA 94949
(Address of Principal Executive Offices)

(415) 408-6200
(Registrant's telephone number)

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

Title of Each Class	Name of Each Exchange on Which Registered
Common Stock, $0.001 par value	The NASDAQ Global Market
Preferred Share Purchase Rights	

Securities registered under Section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes No

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes No

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

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

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company.

Large accelerated filer Accelerated filer Non-accelerated filer Smaller reporting company

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act.) Yes No

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant as of June 30, 2014 (the last business day of the registrant's most recently completed second quarter) was $714.1 million.

The number of shares of the registrant’s common stock outstanding, par value $0.001, on February 27, 2015 was 69,144,463.

The documents incorporated by reference are as follows: Portions of the registrant’s definitive Proxy Statement to be filed with the Securities and Exchange Commission under Regulation 14A within 120 days after the end of registrant’s fiscal year covered by this Annual Report are incorporated by reference into Part III.

RAPTOR PHARMACEUTICAL CORP.

2014 Form 10-K Annual Report

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FORWARD-LOOKING STATEMENTS

Change in Fiscal Year End

On December 4, 2012, the board of directors of Raptor Pharmaceutical Corp., or the "Company," approved a change to the Company's fiscal year end from August 31 to December 31. This Annual Report on Form 10-K includes the financial information for 2014 and 2013 which refers to the periods from January 1 to December 31, 2014 and 2013, respectively. The Company previously filed a report on Form 10-K/T, as amended, for the four-month period from September 1, 2012 to December 31, 2012, or the Transition Period. References in this Annual Report on Form 10-K to fiscal years prior to 2013 refer to the period from September 1 through August 31 of such year.

Forward-Looking Statement

In this Annual Report on Form 10-K, in our other filings with the Securities and Exchange Commission, or the SEC, and in press releases and other public statements by our officers throughout the year, we make or will make statements that plan for or anticipate the future. These "forward-looking statements," within the meaning of the Private Securities Litigation Reform Act of 1995, include statements about our future business plans and strategies, as well as other statements that are not historical in nature. These forward-looking statements are based on our current expectations.

In some cases, these statements can be identified by the use of terminology such as "believes," "expects," "anticipates," "plans," "may," "might," "will," "could," "should," "would," "projects," "anticipates," "predicts," "intends," "continues," "estimates," "potential," "opportunity" or the negative of these terms or other comparable terminology. All such statements, other than statements of historical facts, including statements regarding our financial condition, future results of operations, projected revenues and expenses, business strategies, operating efficiencies or synergies, competitive positions, growth opportunities for existing intellectual properties, technologies, products, plans and objectives of management, markets for our securities and other prospective matters, involve substantial risks and uncertainties and constitute forward-looking statements for the purpose of the safe harbor provided by Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. You should not place undue reliance on these statements, which only reflect information available as of the date that they were made. Our business' actual operations, performance, developments and results might differ materially from any forward-looking statement due to various known and unknown risks, uncertainties, assumptions and contingencies, including those described in the section titled "Risk Factors" in Part I, Item 1A of this Annual Report on Form 10-K as well as other documents we file with the SEC. In light of the significant uncertainties inherent in such forward-looking statements, you should not regard the inclusion of this information as a representation by us or any other person that the results or conditions described in those statements or our objectives and plans will be achieved.

All subsequent forward-looking statements attributable to us or any person acting on our behalf are expressly qualified in their entirety by the cautionary statements contained or referred to herein. Unless required by U.S. federal securities laws and the rules and regulations of the SEC, we do not undertake any obligation and disclaim any intention to update or release publicly any revisions to these forward-looking statements after the filing of this Annual Report on Form 10-K to reflect later events or circumstances or to reflect the occurrence of unanticipated events or for any other reason.

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PART I

ITEM 1: BUSINESS

You should read the following discussion in conjunction with our consolidated financial statements as of December 31, 2014, and the notes to such consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

Unless otherwise stated or the context requires otherwise, for the period from and after the effective time of the 2009 Merger (as described below under "Corporate Information"), all references in this Annual Report on Form 10-K to the “Company,” “we,” “our,” “us,” “Raptor” and similar references refer to the company formerly known as TorreyPines Therapeutics, Inc. and now known as Raptor Pharmaceutical Corp. and its direct and indirect wholly-owned subsidiaries Raptor Pharmaceuticals Inc., Raptor European Products, LLC, RPTP European Holdings C.V., Raptor Pharmaceuticals Europe B.V., Raptor Pharmaceuticals France SAS and Raptor Pharmaceuticals Germany GmbH.

Overview

We are a biopharmaceutical company focused on developing and commercializing transformative treatments for people affected by rare and debilitating diseases.

Our product, PROCYSBI® (cysteamine bitartrate) delayed-release capsules, or PROCYSBI, received marketing approval from the U.S. Food and Drug Administration, or FDA, in April 2013 for the management of nephropathic cystinosis in adults and children six years and older. In Europe, PROCYSBI gastro-resistant hard capsules of cysteamine (as mercaptamine bitartrate), received a marketing authorization in September 2013 from the European Commission, or EC, as an orphan medicinal product for the management of proven nephropathic cystinosis in the European Union, or EU. The EU marketing authorization allows us to commercialize PROCYSBI in the 28 Member States of the EU plus Norway, Liechtenstein and Iceland (which are not EU Member States but are part of the European Economic Area, or EEA). PROCYSBI received seven and ten years of market exclusivity due to its designation as an orphan drug in the United States and the EU, respectively. We achieved first commercial sales of PROCYSBI in the United States in June 2013 and in the EU, specifically in Germany, in April 2014.

As of December 31, 2014, insurers of U.S. commercial patients reimburse Raptor for PROCYSBI therapy at a Wholesale Acquisition Cost, or WAC, price for PROCYSBI of $16,650 per bottle of 250 75-mg capsules and $3,996 per bottle of 60 25-mg capsules. Prices for PROCYSBI therapy vary among patients because doses are individually based on a patient’s weight. In September 2013, we executed an agreement to participate in the U.S. State Medicare/Medicaid rebate program, which will be reflected in our net revenues in mandatory rebates on reimbursements for patients receiving state Medicare and Medicaid insurance coverage. As of December 31, 2014, our price to German, Swiss and Austrian pharmacies was €5,850.23 per bottle of 250 75-mg capsules and €468.02 per bottle of 60 25-mg capsules.

Cysteamine Mechanism of Action

Cysteamine, or 2-aminoethanethiol, the active pharmaceutical ingredient in PROCYSBI, is a molecule generated naturally in human cells during the metabolism of cysteine. Cysteamine is used to construct the key enzymatic cofactor involved in energy produced from sugars and lipids. Cysteamine's uniquely reactive properties result in many physiological effects when given in pharmaceutical doses.

· Antioxidation – Cysteamine is known to increase levels of a key cellular antioxidant, glutathione. Glutathione is composed of the amino acids gamma-glutamate, cysteine and glycine. The availability of cysteine is the major rate-limiting factor in glutathione production. Cysteamine may release cysteine in the circulation, or from within the

cell. Cysteamine has been shown to activate the NRF2 pathway, which leads to the increased expression of a wide variety of proteins involved in antioxidation which may help to reduce oxidative stress in CNS, hepatic and mitochondrial disorders.

- Heat shock response induction – Heat shock proteins, or HSPs, are chaperones that play an important role in protein-protein interactions such as folding and assist in the establishment of proper protein conformation. Proper protein folding may also prevent unwanted protein aggregation. By helping to stabilize partially unfolded proteins, HSPs aid in transporting proteins across membranes within the cell. HSPs are typically produced by cells in response to stress or injury, or other metabolic imbalance. HSPs are part of a cell's mechanism for protein maintenance. The presence of cysteamine within a cell has been shown to increase transcription of certain HSPs that are key components to the cell's ability to maintain the integrity of proteins.

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- Anti-fibrosis – Cysteamine blocks TGF- signaling and thereby inhibits the production and proliferation of myofibroblasts. It also inhibits formation of three cross-links in collagen protein, each of which exacerbate formation of fibrotic tissue: gamma-glutamyl peptide bonds, formed by transglutaminase; oxidized lysyl-lysine conjugates, formed by lysyl oxidase; and inter-chain disulfide bonds.

Cysteamine also inhibits transcription of a variety of collagens and basement membrane-related proteins:

- Metal chelation –In vitro studies have shown that cysteamine chelates metals, including copper, zinc and iron. High doses of cysteamine can lead to copper depletion, implying that chelation effects also occur in vivo.
- Induction of DNA repair mechanisms – Cysteamine has been known for over sixty years to mitigate the effects of radiation by upregulating cell cycle checkpoints and repair mechanisms.

MARKETED PRODUCT

PROCYSBI®

PROCYSBI is an approved therapy for the management of nephropathic cystinosis, a rare, life-threatening metabolic lysosomal storage disorder that causes the rapid, toxic accumulation of cystine in all cells, tissues and organs in the body. PROCYSBI capsules contain cysteamine bitartrate in the form of innovative microspheronized beads that are individually coated to create delayed and extended-release properties, allowing patients to maintain consistent therapeutic systemic drug levels over a 12-hour dosing period. The enteric-coated beads are pH sensitive and bypass the stomach for dissolution and absorption in the more alkaline environment of the proximal small intestine. Randomized controlled clinical trials and extended treatment with PROCYSBI therapy demonstrated consistent cystine depletion as monitored by levels of the biomarker (and surrogate marker), white blood cell cystine.

About Nephropathic Cystinosis

There are approximately 500 patients diagnosed with cystinosis living in the United States and an estimated 2,000 worldwide. Nephropathic cystinosis comprises 95% of known cases of cystinosis. In these patients, elevated cystine leads to cellular dysfunction and death; without treatment, the disease is usually fatal by the end of the first decade of life. Cystinosis is progressive, eventually causing irreversible tissue damage and multi-organ failure, including kidney failure, blindness, muscle wasting and premature death. Nephropathic cystinosis is usually diagnosed in infancy after children present with symptoms including markedly increased urination, thirst, dehydration, gastrointestinal distress, failure to thrive, rickets, photophobia and kidney symptoms specific to Fanconi syndrome. Management of cystinosis requires lifelong therapy.

Cystine depletion is the only approved treatment strategy for nephropathic cystinosis. Committed adherence and persistence to cystine depletion therapy is critical to achieve optimal clinical outcomes. Failure to adhere to prescribed dosing of cystine depletion therapy results in disease progression, including kidney failure leading to dialysis and kidney transplantation, muscle wasting and in most cases, premature death. Even brief interruptions in daily therapy can permit toxic accumulation of cystine, exposing tissues to renewed, progressive deterioration.

In addition to the population of patients who have already been identified, we believe that a number of patients with end-stage renal disease have their condition as a result of undiagnosed late-onset nephropathic cystinosis, and would benefit from treatment with PROCYSBI. In October 2013, we executed a collaboration agreement with DaVita Clinical Research to screen blood samples from U.S. patients with end-stage renal disease in an effort to identify patients with unrecognized late-onset nephropathic cystinosis and who could potentially be candidates to receive PROCYSBI therapy.

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CLINICAL DEVELOPMENT

RP103 Clinical Development

Huntington's Disease

Huntington’s disease, or HD, is a rare, inherited neurodegenerative disorder caused by an autosomal dominant mutation in a gene called huntingtin. The huntingtin gene encodes a protein that is also called "huntingtin." Expansion of a CAG triplet repeat beyond the normal range within the huntingtin gene results in a mutant form of the protein, which gradually damages cells in the brain. HD causes neuronal degeneration in the cerebral cortex and basal ganglia, which play a key role in movement and behavior control. The cumulative damage to these areas results in the hallmark symptoms of HD: a triad of movement, cognitive and neuropsychiatric symptoms which progress gradually in severity over 15-20 years, eventually causing severe physical and mental disability and premature death. The symptoms of HD usually become evident between the ages 35-44 years, but the onset can also begin from childhood to late life (>75 years). The treatment options for HD patients are very limited, with no approved drugs that modify disease course. Recommended treatment strategies consist of drugs for symptomatic relief of chorea, an involuntary motor system (with tetrabenazine, XENAZINE®, approved by FDA) and mood disorder associated with HD as well as a variety of physical, occupational and dietary therapies.

RP103 as a Treatment for Huntington's Disease

RP103, enteric-coated delayed-release cysteamine bitartrate, is currently being evaluated as a treatment for HD. Centre Hospitalier Universitaire, or CHU, d'Angers, France, is conducting the Phase 2/3 clinical trial of RP103. This 36-month clinical trial comprises an 18-month blinded, randomized, placebo-controlled phase followed by an 18-month open-label phase in which all patients transition to RP103. The primary endpoint of the trial is change from baseline of the Total Motor Score, or TMS, of the Unified Huntington's Disease Rating Scale, or UHDRS at 18 months for RP103 vs. placebo groups. TMS, a validated rating scale, is comprised of approximately 15 different measurements that evaluate gross and small motor function in patients with HD. Chorea is one of two involuntary measurements included in the TMS. The Phase 2/3 trial commenced in October 2010, with full enrollment achieved in June 2012. The study enrolled primarily Stage 1 patients showing early disease symptoms with a UHDRS TMS, Score ≥ 5, Total Functional Capacity, or TFC, > 10 and a CAG repeat > 38. Due to the length of the study and the characteristic continuous progression of the disease, patients were allowed to continue their normal medication regime including taking antidepressants and tetrabenazine.

In February 2014, we announced top line results from the planned 18-month analysis of the study. A total of 96 patients with HD were randomized to treatment with RP103 or placebo. A total of 89 patients completed the initial 18-month phase. In the primary analyses (intention to treat population), the change from baseline to month 18 in mean UHDRS TMS was 6.51 in the placebo group and 4.91 in the RP103 group. The between group difference was not statistically significant (p=0.3545).While the results did not reach statistical significance, an overall positive trend was observed.

Patients were not stratified in the study based on concomitant medication use at baseline. We performed post-hoc statistical analyses to assess whether the TMS results were impacted by the effect of tetrabenazine on chorea. In 66 patients not taking tetrabenazine (32 under placebo and 34 under RP103), the results showed a statistically significant difference in the change in total motor score of 2.84 points of progression in the RP103 treatment arm versus 6.78 for the placebo group (p= 0.03).

There were no new or unusual variations from RP103's clinical safety profile with 48 of 52 patients experiencing at least one adverse event, or AE, during the 18-month interim evaluation versus 38 of 44 under placebo. There were slightly more patients under RP103 than under placebo reporting at least one gastrointestinal AE (61.5% RP103

versus 45.5% placebo), mostly nausea, vomiting, abdominal pain, constipation, headache and breath odor. There were five patients treated with RP103 who experienced serious adverse events, or SAEs, compared with four patients treated with placebo. As of the 18-month time point, seven patients discontinued treatment, six in the RP103 arm and one in placebo. Three patients receiving RP103 discontinued for SAEs including one for lymphopenia, one for repetitive faintness and one for elevated liver enzymes. One SAE in the placebo group, anxiety, resulted in discontinuation.

Under our amended collaboration agreement with CHU d'Angers, we supply RP103 and placebo capsules for the clinical trial and open-label extension study and fund the third-party statistical analysis of clinical trial data in exchange for regulatory and commercial rights to the clinical trial data. Clinical expenses of the study are covered by a grant from the Programme Hospitalier de Recherche Clinique, which is funded by the French government.

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In 2008, we received FDA orphan drug designation for cysteamine formulations, including RP103, for the potential treatment of HD. In July, 2014 we received orphan designation from the European Commission for cysteamine bitartrate for the treatment of HD.

RP103 Mechanism in Huntington's Disease

In HD, mutant Htt aggregate formation and processing leads to neuronal, mitochondrial, cellular stress and dysfunction and death. The metabolism of cysteamine boosts systemic cysteine, which may induce several beneficial stress responses, including the production of glutathione, that in aggregate reduce cellular oxidative stress. A major deficiency of cystathionine c-lyase (CSE), the principal generator of endogenous cysteine from cystathionine, has been shown to mediate neurodegeneration in HD. The ability of CSE and cysteine to reverse oxidative stress and lethality in HD cells suggests that cysteine supplementation and intracellular mobilization through cysteamine therapy might be beneficial in treating HD. Through inhibition of intracellular enzymes, such as transglutaminase, cysteamine inhibits protein aggregation, which are known to form in HD. Cysteamine also increases transcription and production of certain heat shock proteins, which may assist in clearing or repairing misfolded Htt and other proteins in neuronal cells. Cysteamine and its dimer cystamine have been shown in preclinical studies to increase levels of brain derived neurotropic factor, or BDNF. BDNF is induced by cortical neurons and helps support survival, growth and differentiation of new neurons and synapses. Two master genes, huntingtin, or Htt, and huntingtin-associated protein, or Hap1, govern BDNF axonal transport and secretion. Expression of the Bdnf gene is reduced in both Alzheimer's and HD patients, and HD patients are believed to be deficient in BDNF. The Bdnf gene may play a role in the regulation of stress response and in the biology of mood disorders. Finally, cysteamine's metal-chelating properties may assist in removing excess copper, a metal that has shown increased accumulation in brains of people with HD as well as other neurodegenerative disorders.

Non-alcoholic Steatohepatitis in Children

Non-alcoholic steatohepatitis, or NASH, is a severe form of non-alcoholic fatty liver disease, or NAFLD, a progressive liver disease associated with deposition of triglycerides in the hepatocytes, in individuals who do not consume hepatotoxic amounts of alcohol. NAFLD is commonly associated with elements of metabolic syndrome, such as obesity, diabetes mellitus and hypertriglyceridemia. Additional factors include family history of diabetes and high blood lipids in people who are not obese. NAFLD refers to a spectrum of conditions ranging from simple fat accumulation in the liver to steatohepatitis, which can lead to cirrhosis, and increase the risk for hepatocellular carcinoma:

- Non-alcoholic fatty liver disease, or NAFLD – A benign condition with simple fat accumulation within liver cells (hepatic steatosis).
- Non-alcoholic steatohepatitis, or NASH – 10% to 15% of patients with NAFLD progress to NASH, an aggressive form of NAFLD characterized by hepatic steatosis and inflammation with hepatocyte injury (ballooning) with or without fibrosis.
- Cirrhosis – 15% to 25% of patients with NASH progress to cirrhosis, usually over a period of 10 to 20 years. Cirrhosis is characterized by the replacement of healthy liver tissue with fibrosis and scar tissue, leading to loss of liver function. NASH cirrhosis is a key risk factor for development of hepatocellular carcinoma, or HCC.

NAFLD and NASH prevalence are increasing along with the rise of obesity. NASH is now among the most common reasons why patients are referred for liver transplantation.

According to the World Gastroenterology Organization Global Guidelines, the prevalence of NAFLD in children is about 15% in the United States and western countries. Many of these children progress to NASH. NAFLD and NASH are underdiagnosed in children often due to the initial asymptomatic nature of the disease, lack of recognition, screening or appreciation of associated complications by healthcare providers. Children may not be recognized as

obese during office visits and age-appropriate norms for body mass index may go unacknowledged. Liver disease is screened by measuring serum alanine aminotransferase, or ALT, and aspartate aminotransferase, or AST, starting at 10 years old in obese children, and in children with a body mass index of 85th to 94th percentile with other risk factors.

Currently there are no approved drug treatment options for NAFLD or NASH. Disease management strategies include recommendations for lifestyle changes in diet, exercise and weight reduction.

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RP103 as a Treatment for NASH in Children

In 2010, a single arm Phase 2a clinical trial was conducted to examine the effects of a prototype of RP103 (twice daily enteric coated cysteamine) as a treatment for NASH in children. Results of this trial with a prototype of RP103 showed that patients exhibited a marked decline in serum transaminase levels during the treatment period of 26 weeks. Seven of 11 juvenile NASH patients entering the study with elevated ALT and AST achieved more than 50% reduction in ALT and six of 11 reduced their ALT levels to normal range. AST levels were also improved, with patients averaging 41% reduction by the end of the 26-week treatment phase. This reduction in serum liver enzymes was largely sustained during the 6-month post-treatment monitoring phase. Other important liver function biomarkers improved significantly, suggesting potential improvements in hepatic histopathology. These markers included reduced levels of cytokeratin 18, or CK-18, a potential serum marker of disease activity in NASH, which decreased by an average of 45%. Adiponectin levels showed a positive increase by an average of 35% during the treatment period. Reduced adiponectin levels are thought to be a marker of the pathogenesis and progression of NASH. Overall, the drug was well tolerated and adverse events were predominantly gastrointestinal and mild in nature.

In June 2012, we announced the dosing of the first patient in a Phase 2b clinical trial – Cysteamine Bitartrate Delayed-Release for the Treatment of Non-alcoholic Fatty Liver Disease in Children, or CyNCh, which is evaluating the safety and efficacy of RP103 as a potential treatment of NASH in children. The clinical trial is being conducted under a Cooperative Research and Development Agreement, or CRADA, with the National Institute of Diabetes and Digestive and Kidney Diseases, or NIDDK, part of the National Institutes of Health, or NIH. Upon full enrollment in January 2014, 169 patients were enrolled at 10 U.S. centers in the NIDDK-sponsored NAFLD Clinical Research Network.

Raptor and NIDDK share the costs of conducting the CyNCh clinical trial. The primary objective of this randomized, multicenter, double-blind, placebo-controlled Phase 2b clinical trial is to evaluate whether 52 weeks of RP103 treatment reverses liver tissue damage caused by NASH as measured by changes in NAFLD Activity Score, or NAS, a histological rating scale of disease activity (based on scoring lobular inflammation, hepatocyte ballooning and steatosis from a liver biopsy), in conjunction with no worsening of liver tissue fibrosis. Secondary endpoints include blood markers for liver health including ALT and AST, antioxidation biomarkers, imaging, as well as safety and tolerability. Top line clinical trial results for this study are anticipated mid-year 2015.

RP103 Mechanism in NASH

Cysteamine's potent antioxidative properties, including the increased production of glutathione, may reduce oxidative damage that results from excessive accumulation of fats in liver cells. In addition, cysteamine's anti-fibrotic activity, including inhibiting the production of transglutaminase, may play a role in stabilizing or even reducing the liver fibrosis that occurs in severe cases of NASH.

Mitochondrial Disorders including Leigh Syndrome

Leigh syndrome is a severe neurological disorder caused by genetic defects in mitochondrial or nuclear DNA affecting respiratory chain function that typically results in death within the first decade of life. The condition causes increased production of reactive oxygen species that disrupt mitochondrial electron transport and affect cellular function in a variety of tissues. Typically observed during the first year of life, Leigh syndrome is characterized by a failure to thrive, lack of coordination, involuntary and sustained muscle contraction, muscle wasting and multiple organ failure. The incidence of Leigh syndrome in the United States is estimated to be 1 in 40,000 newborns.

RP103 as a Treatment for Mitochondrial Disorders including Leigh Syndrome

In June 2014, we initiated a Phase 2 study in the United States designed to evaluate the safety, tolerability and efficacy of RP103 as a potential treatment for Leigh syndrome and other mitochondrial disorders. RP103 potentially increases mitochondrial glutathione which may act as a scavenging agent of reactive oxygen species and thereby reduce the mitochondrial oxidative stress typically associated with these disorders.

The clinical plan includes an open label, 24 week, Phase 2/3 study in 24 patients (up to a maximum of 32 patients). Patients with Leigh syndrome are expected to comprise two-thirds of the enrolled population in the study. Based on an adaptive design statistical plan, we will conduct interim analyses after 4 patients and again after 12 patients have completed the study to determine final sample size. The primary endpoint of the study will be the change from baseline in the Newcastle Pediatric Mitochondrial Disease Scale, or NPMDS, at 24 weeks. Secondary endpoints will include observations of myopathy, dystonia, seizures, motor development, dyskinesia, quality of life and activities of daily living. Interim results from the clinical trial are expected by the end of 2015.

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Other Clinical-Stage Product Candidates

Convivia™ for ALDH2 Deficiency

We are developing Convivia, our proprietary oral formulation of 4-methylpyrazole, or 4-MP, for the potential treatment of acetaldehyde toxicity resulting from ALDH2 deficiency, an inherited metabolic disorder affecting a material percent of East Asian populations.

In June 2010, we entered into an agreement with Uni Pharma Co., Ltd., or Uni Pharma, pursuant to which we granted Uni Pharma an exclusive license under our intellectual property portfolio relating to Convivia, including method of use and formulation patents. Under this agreement, Uni Pharma is responsible for clinical development, registration and commercialization of Convivia in Taiwan.] We continue to seek partners in other Asian countries to which we may license Convivia in the future for such purposes.

Preclinical Product Candidates

Our preclinical programs include our cysteamine dioxygenase, or ADO, program, to improve treatment of diseases for which cysteamine is therapeutic and our HepTide™ program to treat hepatocellular carcinoma and other cancers susceptible to induced lysosomal storage.

Future Activities

We expect that our near-term efforts will be focused on:

- Increasing market penetration and sales of PROCYSBI and providing comprehensive reimbursement and adherence support to commercial patients in the United States;
- Accelerating the launch of PROCYSBI in additional countries in the EEA;
- Increasing market penetration and sales in Germany, Austria and Switzerland;
- Negotiating pricing and reimbursement in specific European countries and launching PROCYSBI in additional EU countries and markets in 2015;
- Continuing a clinical trial to evaluate PROCYSBI in cystinosis patients that are cysteamine-naïve, as well as other supporting trials in underdeveloped markets;
- Developing select global markets with significant numbers of known cystinosis patients;
- Screening for undiagnosed and unidentified late-onset adult nephropathic cystinosis patients;
- Supporting clinical programs and developing clinical and regulatory strategies for the use of RP103 as a potential treatment of HD;
- Prepare for regulatory interactions to determine the clinical regulatory path forward for RP103 for the potential treatment of NASH in children;
- Supporting clinical programs evaluating RP103 for the potential treatment of mitochondrial disorders;
- Supporting our novel preclinical programs;
- Identifying promising in-licensing product and drug development candidates; and
- Continuing the development of our RP103 clinical pipeline in other indications.

Corporate Information

We are incorporated under the laws of the State of Delaware and our business was founded in May 2006. Our principal executive office is located at 7 Hamilton Landing, Suite 100, Novato, CA 94949. Our phone number is (415) 408-6200.

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Corporate History

In September 2009, our subsidiary merged with and into Raptor Pharmaceuticals Corp., a Delaware corporation, or RPC, pursuant to which the stockholders of RPC received shares of our common stock in exchange for their shares of stock and RPC survived as our wholly-owned subsidiary. This merger is referred to herein as the 2009 Merger. Immediately prior to the 2009 Merger, we changed our corporate name from "TorreyPines Therapeutics, Inc." to "Raptor Pharmaceutical Corp." At the time of the 2009 Merger, RPC had two principal subsidiaries, Raptor Discoveries, a development-stage research and development company, and Raptor Therapeutics, which focused on developing clinical-stage drug product candidates through to commercialization and, in connection with the 2009 Merger, these two subsidiaries became our subsidiaries. In December 2012, the two principal subsidiaries were merged and currently operate under the name Raptor Pharmaceuticals Inc. Due to the amount of our stock issued to the stockholders of RPC in the 2009 Merger, RPC was treated as the "accounting acquirer" in the merger, and its board of directors and officers managed and operated the combined company. In December 2011, we merged RPC with and into us and it ceased to exist as a separate company. TorreyPines Therapeutics was incorporated in July 1997 under the name "Axonyx, Inc." and RPC was incorporated in May 2006 under the name "Highland Clan Creations Corp."

Intellectual Property

IP Protection for RP103 for Cystinosis and Other Indications

We seek to protect our proprietary technology and other intellectual property that we believe is important to our business, including by seeking, maintaining and defending patents. We also rely on trade secrets and know-how to protect our business. We own certain of these intellectual property rights and have obtained licenses under other of our intellectual property rights.

Our intellectual property portfolio is directed to the composition of matter, or COM, the method of use, or MOU, and the composition for use, or CFU, of a formulation/pharmaceutical composition for our product candidates, and other proprietary technologies and processes related to our product development candidates. As of February 18, 2015, our patent portfolio included the following patents and patent applications, which we have exclusively licensed from third parties, along with any patents that may issue from these patents and applications in the future:

- Approximately four issued patents and two pending patent application in the United States, and eight issued patents and 26 pending patent applications in other jurisdictions, such as Europe, Australia, China and Japan directed to the formulation/composition, the MOU, and the CFU, of RP103 for cystinosis, metabolic and neurodegenerative conditions (including NASH) and other indications, to which we have an exclusive, worldwide license from the University of California, San Diego, or UCSD. These patents will expire in 2027 and 2028, and additional patents issuing from these patent applications or others that may be filed, if they issue, will expire after the standard 20-year term, subject to available patent term adjustments.
- Approximately two issued patents in the United States directed to the MOU of transglutaminase inhibitors (a class of molecules which includes cysteamine) to treat HD and other neurodegenerative diseases mediated by transglutaminase, or other diseases associated with CAG repeat expansion, to which we have an exclusive, worldwide license from Yeda Research and Development Company Limited (Israel), Niigata University (Japan) and Niigata TLO Inc. (Japan). These patents will expire in 2019.
- Approximately two patent applications pending in the United States directed to the MOU of cysteamine and related compounds for the treatment of parasitic diseases, including malaria, in combination with the current standard of care, artemisinin, to which we have an exclusive, worldwide license from the McGill UniversityPatents issuing from these patent applications or others that may be filed, if they issue, will expire after the standard 20-year term, projected to expire in 2031, subject to available patent term adjustments.

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Approximately one patent application pending in the United States and ten patent applications pending in other jurisdictions, such as Europe, Australia, China and Japan, directed to the MOU of cysteamine and related compounds for the treatment of Parkinson's disease, to which we have an exclusive, worldwide license from the Université Laval. Patents issuing from these patent applications or others that may be filed, if they issue, will expire after the standard 20-year term, projected to expire in 2031, subject to available patent term adjustments.

- Approximately one patent application pending in the United States and five patent applications pending in other jurisdictions, such as Australia, Canada and Mexico, directed to the MOU of cysteamine and related compounds for the treatment of tissue fibrosis, to which we have an exclusive, worldwide license from the Seattle Children's Research Institute. Patents issuing from these patent applications or others that may be filed, if they issue, will expire after the standard 20-year term, projected to expire in 2031, subject to available patent term adjustments.

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- Approximately one patent application in the United States and 14 patent applications pending in other jurisdictions, such as Europe, Australia, China and Japan, directed to the MOU of cysteamine and related compounds to treat MeCP2 associated disorders including Rett Syndrome, to which we have an exclusive license in all countries worldwide where the patent has availability from the Technology Transfer Accelerator of South Eastern France that represents the French medical research organizations where the technology was invented. Patents issuing from these patent applications or others that may be filed, if they issue, will expire after the standard 20-year term, projected to expire in 2031, subject to available patent term adjustments.
- Approximately one patent application pending in the United States and four patent applications pending in other jurisdictions,Australia, Canada, Korea and Mexico, directed to the MOU of cysteamine and related compounds to treat metastatic cancers (including pancreatic, breast, and hepatocellular cancer among others), to which we have an exclusive, worldwide license from the U.S. Food and Drug Administration, or FDA. Patents issuing from these patent applications or others that may be filed, if they issue, will expire after the standard 20-year term, projected to expire in 2031, subject to available patent term adjustments.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the date of filing the non-provisional application. In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office in granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier-filed patent.

In addition, extensions of the term of a patent that covers an FDA-approved drug are available in the United States, in order to compensate for the patent term lost during the FDA regulatory review process. The Hatch-Waxman Act permits a patent term extension of up to five years beyond the expiration of the patent, based on the length of time the drug is under regulatory review, subject to certain limitations. Similar extensions are available in Europe and other foreign jurisdictions for patents that cover an approved drug. We expect to apply for available patent term extensions for patents covering our product candidates.

Trademarks

Our trademark portfolio consists of several registered U.S. trademarks covering our company name, the name of our products and services programs (which are additionally registered in additional territories as necessary to protect our rights to the name). Our trademark RAPTOR is registered in the United States, in the EU, in Australia, and internationally generally and is currently pending registration in several other countries.

All third-party trademarks and trade names identified in this Annual Report on Form 10-K are the property of their respective owners.

License Agreement with UCSD

In December 2007, by way of a merger with Encode Pharmaceuticals, Inc., we acquired certain patent rights licensed to Encode by UCSD pursuant to a license agreement dated October 2007, later amended in February 2008, amended and restated in December 2012, and further amended in March 2013 and December 2013. Pursuant to this agreement, we obtained an exclusive, worldwide, sublicenseable license under certain patent rights and know-how controlled by UCSD for the commercial development, use and sale, for human therapeutic purposes, of products covered by such patents or incorporating such know-how, including RP103. This license is exclusive with respect to the licensed patent rights and non-exclusive with respect to the licensed know-how. Under the agreement, UCSD is obligated to diligently prosecute and maintain the licensed patent rights, conditioned upon our continued fulfillment of our obligation to reimburse UCSD for related costs incurred.

Pursuant to the license agreement, we are obligated to pay milestone payments (ranging in size for orphan and non-orphan indications), up to an aggregate total of $6,275,000, upon the occurrence of certain specified development-, regulatory- and commercial-related events during the term of the agreement. To date, we have paid UCSD $2.2 million in total milestone payments. We are also obligated to pay UCSD a royalty on commercial net sales of licensed products, on a country-by-country basis, ranging in the low single-digit to mid single-digit percentages, based on whether the licensed product sold is covered by the licensed patent rights in such country, as well as a percentage of sublicensing fees and sublicensing royalties we receive under the agreement, if any. In 2013, we began paying UCSD royalties based upon our net sales of PROCYSBI and are subject to a minimum annual royalty of $15,000 until 2018, and $75,000 thereafter.

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Unless earlier terminated, our license agreement with UCSD will expire upon the later of (i) on a country-by-country basis, the expiration of the last to expire of the licensed patent rights (in the applicable country), and (ii) ten years from the first commercial sale of any royalty-bearing product. We may terminate the agreement at any time upon a specified period of prior written notice to UCSD. In the event of our breach of an obligation under the agreement, which breach is not cured within a specified number of days after receiving notice of such from UCSD, UCSD may terminate the agreement or choose to convert the license into a non-exclusive license. The agreement will immediately terminate if we file a claim asserting that any of the licensed patent rights are invalid or unenforceable.

Orphan Drug Designation

We have been granted Orphan Drug Designation from the FDA for use of PROCYSBI to manage cystinosis, and the use of RP103 to potentially treat HD, pancreatic cancer and Batten Disease. The Orphan Drug Act of 1983 generally provides incentives, including marketing exclusivity, user fee waivers and tax benefits, to companies that undertake development and marketing of products to treat relatively rare diseases, which are defined as diseases for which there is a patient population of fewer than 200,000 persons 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. A drug that receives orphan drug designation may receive up to seven years of exclusive marketing in the United States for that indication, 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. A drug may be entitled to an additional six months of exclusive marketing if it satisfies the requirements for pediatric exclusivity; we have applied for this additional six-month pediatric extension for PROCYSBI. See also “Orphan Designation and Exclusivity” and “Pediatric Studies and Exclusivity” below.

PROCYSBI has also been granted Orphan Drug Designation and awarded 10 years of marketing exclusivity by the EC for treatment of cystinosis, and RP103 has been granted Orphan Drug Designation by the EC for the treatment of HD.

Competition

Cystinosis

Other than PROCYSBI, we are aware of two pharmaceutical products currently approved to treat cystinosis. Cystagon® (immediate-release cysteamine bitartrate capsules), is marketed as a systemic cystine-depleting therapy for cystinosis in the United States by Mylan Pharmaceuticals, and by Orphan Europe in markets outside of the United States. Cystagon was approved by the FDA in 1994 and by EC in 1997. Cystaran® (cysteamine ophthalmic solution) was approved by FDA in 2012 for treatment of corneal crystal accumulation in patients with cystinosis and is marketed by Sigma Tau Pharmaceuticals.

While we believe that PROCYSBI will continue to be well received in the market, Cystagon remains on the market and we expect it will compete with PROCYSBI for the foreseeable future. We are not aware of any pharmaceutical company with an active program to develop an alternative therapy for cystinosis. Academic researchers in the United States and Europe are pursuing potential cures for cystinosis through gene therapy and stem cell therapy, as well as pro-drug and pegylated drug approaches as alternatives to cysteamine bitartrate. We believe that the development timeline to an approved product for these approaches is many years with substantial uncertainty.

Huntington's Disease

We are not aware of any approved available treatments to slow the progression of HD. There is only one approved treatment available for specific symptoms of HD, Xenazine® to treat uncontrollable movements (chorea) that result from the disease. There are several pharmaceutical companies pursuing potential cures and disease modifying treatments for HD, as well as numerous academic and foundation sponsored research efforts. To our knowledge, our product candidate, RP103, is the only compound in clinical development which specifically targets deficient BDNF with the goal of slowing motor deterioration.

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Companies with HD product candidates in development include Auspex, Prana Biotechnology, NeuroSearch, Omeros, Teva/Active Biotech, ISIS/Roche, Eli Lilly & Co. and Pfizer. Several other companies have drug candidates in preclinical development. Additionally, nutritional supplements including creatine and coenzyme Q10 have been investigated as potential treatments for HD. The Huntington Study Group sponsors numerous studies of potential therapies for HD, including coenzyme Q10 and the antibiotic minocycline.

NASH and NAFLD

We are not aware of any currently approved treatment options for NASH or NAFLD. Weight loss, healthy diet, abstinence from alcohol and increased physical activity are typically suggested to slow the progression of NASH and NAFLD. There are numerous therapies being studied for NASH, including obeticholic acid, a farnesoid X receptor (FXR) activator (Intercept Pharmaceuticals), lysyl oxidase-like 2 inhibitor and FXR agonist (Gilead), PPAR alpha and delta inhibitor (Genfit), fatty acid/bile acid (FABC) conjugate (Galmed Pharmaceuticals), CCR2/CCR5 inhibitor (Tobira Therapeutics), caspase inhibitor (Conatus Pharma), 5-lipoxygenase inhibitor (MediciNova) and galectin inhibitor (Galectin), as well as anti-oxidants.

ALDH2 Deficiency

We are not aware of any pharmaceutical products currently approved for ALDH2 deficiency, either in the United States or internationally. There are several non-prescription, nutritional supplements available which purport to mitigate the side effects that result from drinking by people with ALDH2 deficiency. Although we are not aware of any study which has demonstrated the efficacy of such non-pharmaceutical alternatives, these products may compete with our ALDH2 deficiency product candidate if it is approved for marketing.

Government Regulations of the Biotechnology Industry

Human therapeutic products are subject to extensive regulation by governmental authorities in the United States and foreign countries. Governmental authorities govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting, sampling, and import and export of pharmaceutical products. The nature and extent to which such regulation will apply to us will vary depending on the nature of any drug product candidates developed. Failure to comply with applicable governmental requirements may subject a company to a variety of administrative or judicial sanctions, such as refusal to approve pending applications, a clinical hold, warning letters, recall or seizure of products, partial or total suspension of production, withdrawal of the product from the market, injunctions, fines, civil penalties or criminal prosecution.

Governmental agency approval is required before any new unapproved drug or dosage form, including a new use of a previously approved drug, can be marketed in each jurisdiction in which the product is marketed. We anticipate that all of our drug product candidates will require regulatory approval by governmental agencies prior to commercialization.

In particular, human therapeutic products are subject to rigorous preclinical and clinical testing and other approval procedures of the FDA and similar regulatory authorities in other countries. Various federal statutes and regulations also govern or influence testing, manufacturing, safety, labeling, storage, record-keeping and marketing related to such products. The process of obtaining these approvals and the subsequent compliance with the appropriate federal statutes and regulations requires substantial time and financial resources.

Before obtaining regulatory approvals for the commercial sale of any of our products under development, we must demonstrate through preclinical studies and clinical trials that the product is safe and efficacious for use in each target indication. The results from preclinical studies and early clinical trials might not be predictive of results that would be

obtained in large-scale testing. Our clinical trials might not successfully demonstrate the safety and efficacy of any product candidates or result in marketable products, and failure can occur at any point in the testing process.

In order to clinically test, manufacture and market products for therapeutic use, we will have to comply with mandatory procedures and safety and effectiveness standards established by various regulatory bodies. In the United States, the Public Health Service Act and the Federal Food, Drug, and Cosmetic Act, as amended, or FDCA, and the regulations promulgated thereunder, and other federal and state statutes and regulations govern, among other things, the testing, manufacture, labeling, storage, record keeping, approval, advertising, and promotion of our current and proposed product candidates. Product development and approval within this regulatory framework takes a number of years and involves the expenditure of substantial resources.

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The steps required by the FDA before new drug products may be marketed in the United States include:

- Completion of extensive preclinical laboratory and animal studies performed in accordance with the FDA's Good Laboratory Practice, or GLP, regulations;
- The submission to the FDA of a request for authorization to conduct clinical trials in an investigational new drug application, or IND, which must become effective before clinical trials may commence;
- Approval by an independent institutional review board, or IRB, or ethics committee representing each clinical site before each clinical study may be initiated;
- Completion of adequate and well-controlled human clinical trials to establish and confirm the safety and efficacy of a drug candidate for the proposed indication;
- Completion of process validation, quality product release and stability;
- Submission to the FDA of a new drug application, or NDA, for the drug candidate for marketing approval;
- Potential review of the product application by an FDA advisory committee, where appropriate and if applicable;
- Satisfactory completion of an FDA pre-approval inspection of the manufacturing facilities where the proposed product is produced to assess compliance with the FDA's current Good Manufacturing Practice, or cGMP, requirement and to assure that the facilities, methods and controls are adequate to preserve the drugs' identity, strength and purity; and
- Review and approval of the NDA by the FDA before the product may be sold commercially.

The pre-clinical and clinical testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that approvals for our product candidates will be granted on a timely basis, if at all. Preclinical testing includes laboratory evaluation and characterization of the safety and efficacy of a drug and its chemistry, formulation, stability and toxicity, as well as animal studies to assess the characteristics and potential safety and efficacy of the product. Preclinical testing results are submitted to the FDA as a part of an IND. Some pre-clinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises concerns or questions relating to one or more proposed clinical trials and places a trial on clinical hold, including concerns that human research subjects will be exposed to unreasonable health risks. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, the submission of an IND may not result in FDA authorization to commence a clinical trial. A separate submission to an existing IND must also be made for each successive clinical trial conducted during product development. Further, an independent IRB, covering each site proposing to conduct the clinical trial must review and approve the plan for any clinical trial and informed consent information for subjects before the trial commences at that site and it must monitor the study until completed.

Clinical trials involve the administration of an investigational drug to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial. Sponsors of clinical trials generally must register and report, at the NIH-maintained website ClinicalTrials.gov, key parameters of certain clinical trials. For purposes of an NDA submission and approval, human clinical trials are typically conducted in the following sequential phases, which may overlap or be combined. Phase 1 represents the initial administration of the drug to a small group of humans, either patients or healthy volunteers, typically to test for safety (adverse effects), dosage tolerance, absorption, distribution, metabolism, excretion and clinical pharmacology, and, if possible, to gain early evidence of effectiveness. Phase 2 involves studies in a small sample of the actual intended patient population to assess the efficacy of the drug for a specific indication, to determine dose tolerance and the optimal dose range and to gather additional information relating to safety and potential adverse effects. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more extensive Phase 3 clinical trials. Once an investigational drug is found to have some efficacy and an acceptable safety profile in the targeted patient population, Phase 3 studies are initiated to further establish clinical safety and efficacy of the therapy in a broader sample of the general patient population, in order to determine the overall risk-benefit ratio of the drug and to provide an adequate basis for any physician labeling. During all clinical studies, we must adhere to GCP or good clinical

practices, standards. The results of the research and product development, manufacturing, preclinical studies, clinical studies and related information are submitted in an NDA to the FDA.

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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. 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 process of completing clinical testing and obtaining FDA approval for a new drug is likely to take a number of years and require the expenditure of substantial resources. If an application is submitted, there can be no assurance that the FDA will review and approve the NDA.

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 requesting approval to market the product for one or more indications. Under federal law, the submission of most NDAs is subject to a substantial application user fee. Applications for orphan drug products are exempt from the NDA user fees, unless the application includes an indication for other than a rare disease or condition.

An NDA 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.

Under federal law, the submission of an NDA is subject to a substantial application user fee, and the manufacturer and/or sponsor under an approved NDA are also subject to annual product and establishment user fees. The FDA has 60 days from its receipt of an NDA to determine whether the application will be accepted for filing based on the agency’s threshold determination that it is sufficiently complete to permit substantive review. The FDA may request additional necessary information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information and may be subject to payment of additional user fees. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission has been accepted for filing, the FDA begins an in-depth substantive review.

The FDA's goal is to review the application within 10 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. In addition, an application may be referred to an advisory committee, which is a panel of independent experts, to review, evaluate and provide a recommendation to the FDA 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 typically follows such recommendations and considers them carefully when making approval decisions.

Before obtaining FDA approval for each product, the FDA typically will inspect the facility or facilities where the product is manufactured and 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, the FDA will typically inspect one or more clinical sites to assure compliance with GCP requirements. Following approval, each product manufacturing establishment must be registered with the FDA and its quality control and manufacturing procedures must continue to conform and adhere at all times to the FDA's cGMP regulations. The FDA and other government agencies regularly inspect manufacturing facilities for compliance with these requirements. If, as a result of these inspections, the FDA

determines that any equipment, facilities, laboratories or processes do not comply with applicable FDA regulations and conditions of product approval, the FDA may seek civil, criminal or administrative sanctions and/or remedies against us, including the suspension of the manufacturing operations. Manufacturers must expend substantial time, money and effort in the area of production and quality control to ensure full technical compliance with these standards.

In some cases, the FDA may condition approval of an NDA for a product candidate on the sponsor's agreement to conduct additional clinical trials to further assess the drug's safety and effectiveness after NDA approval. Such post-approval trials are typically referred to as Phase 4 studies. In addition, even after initial FDA approval has been obtained, further studies would be required to gain approval for the use of a product as a treatment for clinical indications other than those for which the product was initially tested and approved. Once an NDA is approved, a product will be subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to drug/device listing, recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. Results of post-marketing programs, including Phase 4 clinical studies or post-market surveillance, might limit or expand the further marketing of the products. Further, if there are any modifications to the drug, including changes in indication, manufacturing process, labeling or a change in manufacturing facility, submission and approval of an NDA supplement might be required. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and generally require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP or QSR 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 cGMP or QSR compliance.

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Failure to comply with applicable FDA requirements may result in a number of consequences that could materially and adversely affect us. Failure to adhere to approved trial standards and GCPs in conducting clinical trials could cause the FDA to place a clinical hold on one or more studies which would delay research and data collection necessary for product approval. Noncompliance with GCPs could also have a negative impact on the FDA's evaluation of an NDA. Failure to adhere to GCPs, cGMPs and other applicable requirements could result in FDA enforcement action and in civil and criminal sanctions, including but not limited to fines, seizure of product, refusal of the FDA to approve product approval applications, withdrawal of approved applications, and prosecution. 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 Risk Evaluation and Mitigation Strategies, or REMS, program.

The FDA strictly regulates marketing, labeling, advertising, and promotion of products that are placed on the market pursuant to a number of complex regulations which include, among others, standards for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities, and promotional activities involving the internet. 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. Indeed, the FDA has very broad enforcement authority under the FFDCA, and failure to abide by these regulations can result in penalties, including the issuance of a warning letter directing entities to correct deviations from FDA standards, a requirement that future advertising and promotional materials be pre-cleared by the FDA, and state and federal civil and criminal investigations and prosecutions.

Whether or not FDA approval has been obtained, approval of a product by regulatory authorities in foreign countries must be obtained prior to the commencement of marketing of the product in those countries. The requirements governing the conduct of clinical trials and product approvals vary widely from country to country, and the time required for approval might be longer or shorter than that required for FDA approval. Although there are some procedures for unified filings for some European countries, in general, each country at this time has its own procedures and requirements. There can be no assurance that any foreign approvals would be obtained.

In addition to the regulatory framework for product approvals, we and our collaborative partners must comply with federal, state and local laws and regulations regarding occupational safety, laboratory practices, the use, handling and disposition of radioactive materials, environmental protection and hazardous substance control, and other local, state, federal and foreign regulations. All facilities and manufacturing processes used by third parties to produce our drug candidates for clinical use in the United States must conform with cGMPs. These facilities and practices are subject to periodic regulatory inspections to ensure compliance with cGMP requirements. Their failure to comply with applicable regulations could extend, delay, or cause the termination of clinical trials conducted for our drug candidates or of manufacturing and sale of any of our products approved for sale. We cannot accurately predict the extent of government regulation that might result from future legislation or administrative action.

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. 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 clinical studies submitted in an NDA, upon the request of an applicant, the FDA may grant the NDA 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 10 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.

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Under the accelerated approval program, the FDA may approve an NDA 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.

European Union Drug Review and Approval

In the EEA (which is comprised of the 28 Member States of the European Union plus Norway, Iceland and Liechtenstein), medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA. There are two types of MA:

The Community MA, which is issued by the European Commission through the Centralized Procedure, based on the opinion of the CHMP of the EMA, is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, and medicinal products containing a new active substance indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes and auto-immune and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.

National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in other Member States through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure.

Under the above described procedures, before granting the MA, the EMA or the competent authorities of the Member States of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

Orphan Drug Designation and Exclusivity

The Orphan Drug Act provides incentives for the development of products intended to treat rare diseases or conditions. Under the Orphan Drug Act, the FDA may grant orphan designation to a drug intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making a drug product available in the United States for this type of disease or condition will be recovered from sales of the product. If a sponsor demonstrates that a drug is intended to treat rare diseases or conditions, the FDA will grant Orphan Drug Designation for that product for the orphan disease indication. Orphan Drug Designation must be requested before submitting an NDA. After the FDA grants Orphan Drug Designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA.

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Orphan Drug Designation provides manufacturers with research grants, tax credits and eligibility for orphan drug exclusivity. If a product that has Orphan Drug Designation subsequently receives the first FDA approval of the active moiety for that disease or condition for which it has such designation, the product is entitled to orphan drug exclusivity, which for seven years prohibits the FDA from approving another product with the same active ingredient for the same indication, except in limited circumstances. If a drug designated as an orphan product receives marketing approval for an indication broader than the orphan indication for which it received the designation, it will not be entitled to orphan drug exclusivity. Orphan exclusivity will not bar approval of another product under certain circumstances, including if a subsequent product with the same active ingredient for the same indication is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand. Further, the FDA may approve more than one product for the same orphan indication or disease as long as the products contain different active ingredients. Moreover, competitors may receive approval of for the same product but for a different indication for which the orphan product has exclusivity. As a result, even if we obtain orphan exclusivity, we may still be subject to competition.

In the EU, the EMA's Committee for Orphan Medicinal Products, or COMP, grants Orphan Drug Designation to promote the development of products that are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions affecting not more than five 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 EU would be sufficient to justify the necessary investment in developing the medicinal product. In the EU, 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.

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.

Pediatric Studies and Exclusivity

NDAs 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. 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 Biologic License Application 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 approve another application relying on the NDA sponsor's data. We have applied for this additional six-month pediatric extension for PROCYSBI.

Hatch-Waxman Amendments and Exclusivity

As an alternative path to FDA approval for modifications to formulations or uses of products previously approved by the FDA, an applicant may submit an NDA under Section 505(b)(2) of the FDCA. Section 505(b)(2) was enacted as part of the Hatch-Waxman Amendments and permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by, or for, the applicant. If the 505(b)(2) applicant can establish that reliance on FDA's previous findings of safety and effectiveness is scientifically appropriate, it may eliminate the need to conduct certain preclinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements, including clinical trials, to support the change from the approved branded reference drug. The FDA may then approve the new product candidate for all, or some, of the label indications for which the branded reference drug has been approved, as well as for any new indication sought by the 505(b)(2) applicant.

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In seeking approval for a drug through an NDA, including a 505(b)(2) NDA, applicants are required to list with the FDA certain patents whose claims cover the applicant's product. Upon approval of an NDA, each of the patents listed in the application for the drug is then published in the Orange Book. Any applicant who files an abbreviated new drug application, or ANDA, seeking approval of a generic equivalent version of a drug listed in the Orange Book or a 505(b)(2) NDA referencing a drug listed in the Orange Book must certify to the FDA that (1) no patent information on the drug product that is the subject of the application has been submitted to the FDA; (2) such patent has expired; (3) the date on which such patent expires; or (4) such patent is invalid or will not be infringed upon by the manufacture, use or sale of the drug product for which the application is submitted. This last certification is known as a paragraph IV certification. A notice of the paragraph IV certification must be provided to each owner of the patent that is the subject of the certification and to the holder of the approved NDA to which the ANDA or 505(b)(2) application refers. The applicant may also elect to submit a "section viii" statement certifying that its proposed label does not contain (or carves out) any language regarding the patented method-of-use rather than certify to a listed method-of-use patent.

If the reference NDA holder and patent owners assert a patent challenge directed to one of the Orange Book listed patents within 45 days of the receipt of the paragraph IV certification notice, the FDA is prohibited from approving the application until the earlier of 30 months from the receipt of the paragraph IV certification expiration of the patent, settlement of the lawsuit or a decision in the infringement case that is favorable to the applicant. The ANDA or 505(b)(2) application also will not be approved until any applicable non-patent exclusivity listed in the Orange Book for the branded reference drug has expired. Specifically, the holder of the NDA for the listed drug may be entitled to a period of non-patent exclusivity, during which the FDA cannot approve an ANDA or 505(b)(2) application that relies on the listed drug. For example, a pharmaceutical manufacturer may obtain five years of non-patent exclusivity upon NDA approval of a new chemical entity, or NCE, which is a drug that contains an active moiety that has not been approved by FDA in any other NDA. An "active moiety" is defined as the molecule or ion responsible for the drug substance's physiological or pharmacologic action. During the five-year exclusivity period, the FDA cannot accept for filing any ANDA seeking approval of a generic version of that drug or any 505(b)(2) NDA for the same active moiety and that relies on the FDA's findings regarding that drug, except that FDA may accept an application for filing after four years if the follow-on applicant makes a paragraph IV certification.

A drug, including one approved under Section 505(b)(2), may obtain a three-year period of exclusivity for a particular condition of approval, or change to a marketed product, such as a new formulation for a previously approved product, if one or more new clinical studies (other than bioavailability or bioequivalence studies) was essential to the approval of the application and was conducted/sponsored by the applicant. Should this occur, the FDA would be precluded from approving any ANDA or 505(b)(2) application for the protected modification until after that three-year exclusivity period has run. However, unlike NCE exclusivity, the FDA can accept an application and begin the review process during the exclusivity period.

Coverage and Reimbursement

The commercial success of PROCYSBI and our drug candidates and our ability to commercialize those products successfully will depend in part on the extent to which governmental payor programs at the federal and state levels, including Medicare and Medicaid, private health insurers and other third-party payors provide adequate coverage and reimbursement. These third-party payors generally develop their own policies as to which drugs they will pay for and the reimbursement levels for the drugs. For example, governmental programs in the United States often require manufacturers to pay certain rebates or otherwise provide discounts to secure coverage of drug products. To control healthcare expenditures generally, in the United States, the EU and other potentially significant markets for PROCYSBI and our drug candidates, government authorities and third party payors are increasingly attempting to limit or regulate the price of medical products and services, particularly for new and innovative products and therapies. The measures taken often have resulted in lower average selling prices. Further, the increased emphasis on managed healthcare in the United States and on country and regional pricing and reimbursement controls in the EU places additional pressure on product pricing, reimbursement and usage, which may adversely affect our future

product sales and results of operations. These pressures can arise from rules and practices of managed care groups, judicial decisions and governmental laws and regulations related to Medicare, Medicaid and healthcare reform, as well as drug coverage and reimbursement policies and pricing in general.

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Some of the additional requirements and restrictions on coverage and reimbursement levels imposed by third-party payors influence the purchase of healthcare services and products. For example, there may be limited coverage to specific drug products on an approved list, or formulary, which might not include all of the FDA-approved drug products for a particular indication. There may also be formulary placements that result in lower reimbursement levels and higher cost-sharing borne by patients. Further, third-party payors are increasingly examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. 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 the FDA approvals. Our products may not be considered medically necessary or cost-effective. Even if a third-party payor determines to provide coverage for a drug product, adequate reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in drug development.

Healthcare legislative proposals to reform healthcare or reduce costs under government insurance programs may also result in lower reimbursement for our drugs and drug candidates or exclusion of our drugs and drug candidates from coverage altogether. The cost containment measures that healthcare payors and providers are instituting and any healthcare reform could significantly reduce our revenues from the sale of PROCYSBI and any of our approved drug candidates. We cannot provide any assurances that we will be able to obtain and maintain third party coverage or adequate reimbursement for PROCYSBI or any of our approved drug candidates in whole or in part.

Healthcare Reform

With respect to legislative reform, in the United States, there have been and continue to be a number of significant legislative initiatives to contain healthcare costs. For example, in March 2010, the Affordable Care Act 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 Affordable Care Act, among other things, subjects biologic products to potential competition by lower-cost biosimilars, addresses a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increases the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extends the rebate program to individuals enrolled in Medicaid managed care organizations, establishes annual fees and taxes on manufacturers of certain branded prescription drugs, and a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer’s outpatient drugs to be covered under Medicare Part D.

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 of 2% per fiscal year, which went into effect in April 2013, due to subsequent legislative amendments to the statute, and will remain in effect through 2024 unless additional Congressional action is taken.

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.

Other Healthcare Laws

We are also subject to healthcare regulation and enforcement by the federal government and the states and foreign governments in which we conduct our business. These laws include, without limitation, state and federal anti-kickback, fraud and abuse, false claims, privacy and security and physician sunshine laws and regulations.

The federal Anti-Kickback Statute prohibits, among other things, any person from knowingly and willfully offering, soliciting, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual, for an item or service or the purchasing or ordering of a good or service, for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs. The Anti-Kickback Statute is subject to evolving interpretations. In the past, the government has enforced the Anti-Kickback Statute to reach large settlements with healthcare companies based on sham consulting and other financial arrangements with physicians. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, 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 federal False Claims Act. The majority of states also have anti-kickback laws which establish similar prohibitions and in some cases may apply to items or services reimbursed by any third-party payor, including commercial insurers.

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Additionally, the civil False Claims Act prohibits knowingly presenting or causing the presentation of a false, fictitious or fraudulent claim for payment to the United States government. Actions under the False Claims Act may be brought by the Attorney General or as a qui tam action by a private individual in the name of the government. Violations of the False Claims Act can result in very significant monetary penalties and treble damages. The federal government is using the False Claims Act, and the accompanying threat of significant liability, in its investigation and prosecution of pharmaceutical and biotechnology companies throughout the country, for example, in connection with the promotion of products for unapproved uses and other sales and marketing practices. The government has obtained multi-million and multi-billion dollar settlements under the False Claims Act in addition to individual criminal convictions under applicable criminal statutes. Given the significant size of actual and potential settlements, it is expected that the government will continue to devote substantial resources to investigating healthcare providers' and manufacturers' compliance with applicable fraud and abuse laws.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, also created new federal criminal statutes that prohibit among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

In addition, a person who offers or transfers to a Medicare or Medicaid beneficiary any remuneration, including waivers of co-payments and deductible amounts (or any part thereof), that the person knows or should know is likely to influence the beneficiary’s selection of a particular provider, practitioner or supplier of Medicare or Medicaid payable items or services may be liable for civil monetary penalties of up to $10,000 for each wrongful act. Moreover, in certain cases, providers who routinely waive copayments and deductibles for Medicare and Medicaid beneficiaries can also be held liable under the Anti-kickback Statute and civil False Claims Act, which can impose additional penalties associated with the wrongful act. One of the statutory exceptions to the prohibition is non-routine, unadvertised waivers of copayments or deductible amounts based on individualized determinations of financial need or exhaustion of reasonable collection efforts. The Office of Inspector General of the Department of Health and Human Services emphasizes, however, that this exception should only be used occasionally to address special financial needs of a particular patient. Although this prohibition applies only to federal healthcare program beneficiaries, the routine waivers of copayments and deductibles offered to patients covered by commercial payers may implicate applicable state laws related to, among other things, unlawful schemes to defraud, excessive fees for services, tortious interference with patient contracts and statutory or common law fraud. To the extent our patient assistance programs are found to be inconsistent with applicable laws, we may be required to restructure or discontinue such programs, or be subject to other significant penalties.

There has also been a recent trend of increased federal and state regulation of payments made to physicians and other healthcare providers. The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the Affordable Care Act, among other things, imposes new reporting requirements on drug manufacturers for payments made by them to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Failure to submit required information may result in civil monetary penalties of up to an aggregate of $150,000 per year (or up to an aggregate of $1 million per year for "knowing failures"), for all payments, transfers of value or ownership or investment interests that are not timely, accurately and completely reported in an annual submission. Drug manufacturers were required to begin collecting data on August 1, 2013 and submit reports to the government by March 31, 2014 and June 30, 2014, and the 90th day of each subsequent calendar year. Certain states also mandate implementation of compliance programs, impose restrictions on drug manufacturer marketing practices and/or require the tracking and reporting of gifts, compensation and other remuneration to physicians.

We may also be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology and Clinical Health Act, or HITECH, and their respective implementing regulations, including the final omnibus rule published on January 25, 2013, imposes specified requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to "business associates," defined as independent contractors or agents of covered entities that create, receive, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways, thus complicating compliance efforts.

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The shifting commercial compliance environment and the need to build and maintain robust and expandable systems to comply with different compliance and/or reporting requirements in multiple jurisdictions increase the possibility that a healthcare company may violate one or more of the requirements. If our operations are found to be in violation of any of such laws or any other governmental regulations that apply to us, we may be subject to penalties, including, without limitation, civil and criminal penalties, damages, fines, the curtailment or restructuring of our operations, exclusion from participation in federal and state healthcare programs and imprisonment, any of which could adversely affect our ability to operate our business and our financial results.

Research and Development

We have an active research and development effort. We plan to focus our research and development efforts in the discovery, research, preclinical and clinical development of our drug candidates in order to provide therapies that we believe will be safer, less intrusive and more effective than current approaches in treating a wide variety of disorders. During the years ended December 31, 2014 and 2013, the four-month transition period ended December 31, 2012 and the fiscal year ended August 31, 2012, we incurred approximately $43.5 million, $29.2 million, $9.0 million, and $21.4 million, respectively, in research and development expenses.

Operating Segment and Geographic Information

Operating segments are components of an enterprise for which separate financial information is available and is evaluated regularly by a company in deciding how to allocate its resources and to assess its performance. We have reviewed how we allocate our resources and analyze performance worldwide and have determined that, because employees work on integrated programs in the United States and in Europe, encompassing all stages of product development and commercialization, we operate in one segment.

Compliance with Environmental Laws

We estimate the annual cost of compliance with environmental laws, comprised primarily of hazardous waste removal, will be nominal.

Employees

As of December 31, 2014, we had 123 full time employees (100 and 23 in the United States and EU, respectively). Of the 123 employees, 75 are sales and marketing and general and administrative personnel and 48 are in manufacturing, quality control and assurance and research and development. Based on our current plan, over the next 12-month period we intend to expand our U.S. and EU employee base across most functions in the Company.

Facilities

Our primary offices are located at 7 Hamilton Landing, Suite 100, Novato, CA 94949. Our main phone number is (415) 408-6200 and our facsimile number is (415) 382-8002. Our European headquarters are located at Naritaweg 165, 1043 BW Amsterdam, Netherlands and we have administrative offices in Utrecht, Netherlands.

Website

Our corporate website is located at www.raptorpharma.com. Any information contained in, or that can be accessed through, our website is not incorporated by reference into this Annual Report on Form 10-K.

Available Information

Our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act may be accessed through the SEC's website at www.sec.gov and on our website at www.raptorpharma.com. Such filings are placed on our website as soon as reasonably practicable after they are filed with the SEC. Our code of business conduct and ethics, audit committee charter, corporate governance and nominating committee charter and compensation committee charter are also posted on our website.

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ITEM 1A: RISK FACTORS

Investing in our common stock involves a high degree of risk. Before deciding whether to invest in our common stock, you should consider carefully the risk factors described below, together with the other information contained in this Annual Report on Form 10-K and other documents we file with the SEC, such as our quarterly reports on Form 10 Q, our current reports on Form 8 K and any public announcements we make from time to time. If any of these risks actually occur, it may materially harm our business, financial condition, operating results or cash flow. As a result, the market price of our common stock could decline, and you could lose all or part of your investment. Additional risks and uncertainties that are not yet identified or that we think are immaterial may also materially harm our business, operating results and financial condition and could result in a complete loss of your investment.

Risks Associated with Commercialization and Product Development

Our revenues currently depend entirely on the commercial success of our lead drug, PROCYSBI, for the management of nephropathic cystinosis.

PROCYSBI is our only product currently approved for marketing, and as a result, our revenue and operating results substantially depend on the commercial success of PROCYSBI. We commenced marketing for PROCYSBI in the United States in June 2013 and Europe in April 2014. We did not have prior experience commercializing therapeutics. In the United States, we are permitted to market PROCYSBI only for the management of nephropathic cystinosis in adults and children six years and older. In September 2013, we received marketing authorization from the European Commission, or EC, to commercialize PROCYSBI for the treatment of proven nephropathic cystinosis in the Economic European Area, or EEA. However, we only recently commenced commercial sales of PROCYSBI in select countries in Europe, and have no assurance of securing reimbursement and subsequently launching in additional countries in the EEA. We believe that our results of operations and, in particular, net product sales of PROCYSBI will affect the trading price of our common stock substantially. If PROCYSBI sales do not meet expectations, our stock price may fluctuate, including a potential and possibly significant decrease.

The successful commercialization of PROCYSBI will depend on several factors, including:

- our ability to provide acceptable evidence of the safety and efficacy of PROCYSBI;
- compliance with regulatory requirements, including fulfilling post-approval commitments;
- our ability to obtain approval by regulatory agencies in other countries, including appropriate product labeling;
- the effect of current and future healthcare laws;
- the manufacture and supply of adequate quantities of PROCYSBI in compliance with current good manufacturing practices, or cGMPs, as needed to meet commercial demand;
- adequate coverage and reimbursement for PROCYSBI from commercial health plans and government health programs, which we refer to collectively as third-party payors;
- our ability to obtain acceptable prices in EEA countries and other select territories, including reimbursement at the country-specific price;
- limitations or warnings currently contained in or as may later be required in approved labeling and the breadth of product labeling or product insert requirements;
- our ability to enter into agreements with wholesalers, distributors and pharmacies on commercially reasonable terms; and
- the development and maintenance of intellectual property and other product protection for PROCYSBI.

If we fail to grow sales of PROCYSBI in existing markets or to successfully commercialize PROCYSBI in other countries within a reasonable time period, we may never become profitable and may be unable to sustain our business, our business, and results of operations and financial condition will be materially adversely affected.

Our ability to generate significant product sales from PROCYSBI is dependent upon market acceptance among physicians, patients, patient families, third-party payors and the healthcare community.

PROCYSBI may not attain or maintain market acceptance among physicians, patients, patient families, third-party payors or the healthcare community compared to the current standard of care and our competitors. We believe that the degree of market acceptance and our ability to generate significant product sales of PROCYSBI will depend on a number of factors, including:

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- the relative efficacy, safety, availability and ease of administration of alternative treatments;
- the price of our product, both in absolute terms and relative to alternative treatments;
- the timing of market introduction of our product relative to competitive drugs;
- the nature of publicity related to our products relative to the publicity related to our competitors' products;
- the prevalence and severity of adverse side effects of PROCYSBI;
- continued patient adherence to therapy;
- availability of coverage from third-party payors;
- provision of affordable out-of-pocket costs to patients and/or other programs to ensure patient access to PROCYSBI; and
- the identification of currently diagnosed and undiagnosed patients and the continued growth of the cystinosis market.

Our efforts to educate patients, physicians, parents, the medical community and third-party payors on the benefits of PROCYSBI may require significant resources and may not be successful. If PROCYSBI does not achieve and maintain significant market acceptance among physicians, patients, patient families, third-party payors or the healthcare community, our business, results of operations and financial condition will be materially adversely affected.

The amount of our product sales of PROCYSBI in the EEA is dependent in part upon the pricing and reimbursement guidelines adopted in each of the EEA countries, which may not be at acceptable levels.

We currently sell PROCYSBI in select EEA countries at the German price. One or more EEA countries may not support our anticipated pricing and reimbursement levels for PROCYSBI, particularly in light of the budget crises faced by a number of countries and third-party payors in the EEA, which would negatively affect revenues from PROCYSBI. The pricing and reimbursement process in EEA countries can be lengthy and involved, and we do not have significant experience with this process. Failure to timely complete the pricing and reimbursement process in the EEA countries will delay our ability to further market PROCYSBI and our ability to derive revenues from that region.

PROCYSBI is, and any other future product candidates, if approved, will be, subject to extensive and ongoing regulatory requirements and continued regulatory review, which will result in significant expense, and we may be subject to penalties and litigation if we fail to comply with regulatory requirements or experience problems with our products.

Even after we achieve regulatory approvals, we are subject to ongoing obligations and continued regulatory review with respect to our manufacturing processes, labeling, packaging, distribution, storage, adverse event reporting, dispensation, advertising, promotion and recordkeeping. These requirements include submissions of safety and other post-marketing information and reports, ongoing maintenance of product registration and continued compliance with good manufacturing practices, or GMPs, good clinical practices, or GCPs, good distribution practices, or GDPs, and good laboratory practices, or GLPs. If we, our products or product candidates or the manufacturing facilities for our products or product candidates fail to comply with applicable regulatory requirements, a regulatory agency may:

- impose restrictions on the marketing or manufacturing of a product, suspend or withdraw product approvals, revoke necessary licenses or suspend product reimbursement;
- impose injunctions, suspensions or revocations of necessary approvals or other licenses;
- issue warning letters, show cause notices or untitled letters describing alleged violations, which may be publicly available;
- suspend any ongoing clinical trials;
- delay or refuse to approve pending applications or supplements to approved applications filed by us;
- refuse to permit drugs or precursor chemicals to be imported or exported to or from the United States;
- suspend or impose restrictions on operations, including costly new manufacturing requirements;
- seize or detain products or require us to initiate a product recall; or

·commence criminal investigations and prosecutions.

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Moreover, existing regulatory approvals and any future regulatory approvals that we obtain will be subject to limitations on the approved indicated uses for which the product may be marketed, the conditions of approval, requirements for potentially costly, post-market testing and requirements for surveillance to monitor the safety and efficacy of the product. In the EEA, the advertising and promotion of pharmaceuticals is strictly regulated. The direct-to-consumer promotion of prescription pharmaceuticals is not permitted, and some countries of the EEA require the notification and/or prior authorization of promotional or advertising materials directed at healthcare professionals. The FDA, EMA, EC and other authorities in the EEA countries strictly regulate the promotional claims that may be made about prescription products, and our product labeling, advertising and promotion are subject to continuing regulatory review. Physicians nevertheless may prescribe our product to their patients in a manner that is inconsistent with the approved label or that is off-label. Positive clinical trial results in any of our RP103 programs increase the risk that immediate-release cysteamine bitartrate may be used off-label in those indications in certain geographic areas due to the lower cost of immediate-release cysteamine bitartrate. If we are found to have improperly promoted off-label uses, we may be subject to significant sanctions, civil and criminal fines and injunctions prohibiting us from engaging in specified promotional conduct.

In addition, engaging in improper promotion of our products for off-label uses in the United States can subject us to false claims litigation under federal and state statutes. These false claims statutes in the United States include the federal False Claims Act, which allows any individual to bring a lawsuit against a pharmaceutical company on behalf of the federal government alleging submission of false or fraudulent claims or causing to present such false or fraudulent claims for payment by a federal program such as Medicare or Medicaid. Growth in false claims litigation has increased the risk that a pharmaceutical company will have to defend a false claim action, pay civil money penalties, settlement fines or restitution, agree to comply with burdensome reporting and compliance obligations and be excluded from Medicare, Medicaid and other federal and state healthcare programs.

The regulations, policies or guidance of regulatory agencies may change and new or additional statutes or government regulations may be enacted that could prevent or delay regulatory approval of our product candidates or further restrict or regulate post-approval activities. For example, the Food and Drug Administration Safety and Innovation Act, or FDASIA, requires the FDA to issue new guidance describing its policy regarding internet and social media promotion of regulated medical products, and the FDA may soon specify new restrictions on this type of promotion. In January 2014, the FDA released draft guidance on how drug companies can fulfill their regulatory requirements for post-marketing submission of interactive promotional media, and though the guidance provided insight into how the FDA views a company’s responsibility for certain types of social media promotion, there remains a substantial amount of uncertainty. We cannot predict the likelihood, nature or extent of adverse government regulation that may arise from pending or future legislation or administrative action, either in the United States or abroad. If we are unable to achieve and maintain regulatory compliance, we may not be permitted to market our drugs, which would adversely affect our ability to generate revenue and achieve or maintain profitability.

If we are unable to expand the use of RP103 and receive regulatory approval for any other indication or for other product candidates, we may delay or terminate some of our product development activities, which would adversely affect the long term value of RP103 or other product candidates and our growth prospects.

The research, testing, manufacturing, labeling, approval, sale, marketing and distribution of drug products, among other things, are subject to extensive regulation by the FDA and other regulatory authorities in the United States and by similar foreign regulatory governmental entities. We are not permitted to market any of our drug product candidates unless we obtain and maintain appropriate pre-market approvals from regulatory agencies in each of the markets in which we intend to market our products. Once approved, we may only market our products for the specific uses that are reflected in the product’s approved labeling. A product’s approved labeling may contain limitations or warnings or may be for different patient populations or for fewer or more limited indications than what we requested in our pre-market approval application, which could result in reimbursement complications, limit access for intended use or limit the commercial profile of the drug. In the United States, we are permitted to market the active

pharmaceutical ingredient of RP103 in the formulation of a final drug product and in the doses approved under the brand name PROCYSBI only for the management of nephropathic cystinosis in adults and children six years and older under the brand name PROCYSBI. We are permitted to market PROCYSBI in the EEA as an orphan medicinal product for the treatment of proven nephropathic cystinosis. We do not have approval of RP103 in any other market nor for any other disease indication. There can be no assurance that we will obtain regulatory approval for any other uses for PROCYSBI or any of our other product candidates or that, even if we obtained additional approvals, we would be able to commercialize the product candidates successfully.

A new drug application, or NDA, submitted to the FDA, or a marketing authorization application, or MAA, submitted to the European Medicine Agency, or the EMA, must be supported by extensive clinical and preclinical data, as well as extensive information regarding chemistry, manufacturing and controls. This information must demonstrate the safety and efficacy of the applicable product candidate for the management of each individual indication to the satisfaction of the applicable regulatory authority. Obtaining approval of an NDA, MAA or any other filing for marketing authorization in a foreign country is an extensive, expensive and uncertain process. The time required to obtain approval by the FDA and comparable foreign authorities is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. The FDA, EC or other regulatory authorities may delay, limit or deny approval of RP103 or our future drug product candidates for many reasons, including:

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- the results of clinical trials may not meet the level of statistical or clinical significance required by regulatory authorities for approval;
- regulatory authorities may disagree with the number, design, size, conduct or implementation of our clinical trials;
- they may change the requirements for approval even after having reviewed and commented on the design for our clinical trials;
- regulatory authorities may not find the data from preclinical studies and clinical trials sufficient to demonstrate that product candidates have adequate clinical and other benefits or adequate safety profiles, even if they achieve their specified endpoints in clinical trials; or they may disagree with our interpretation of data from preclinical studies or clinical trials and require that we conduct additional trials;
- regulatory authorities may not accept data generated at our clinical trial sites;
- regulatory authorities may have difficulties scheduling an advisory committee meeting (or equivalent, if required) in a timely manner, or the advisory committee may recommend against approval of our application or may recommend that the regulatory agency require, as a condition of approval, additional preclinical studies or clinical trials; approval may also be contingent on a Risk Evaluation and Mitigation Strategy, which limits the labeling, distribution or promotion of a drug product;
- regulatory authorities may require additional preclinical or clinical studies or other data prior to granting approval, and we may not be able to generate the required data on a timely basis, if at all;
- regulatory authorities may identify deficiencies in the manufacturing processes or in the facilities of our third-party suppliers and/or contract manufacturers or may require us to manufacture additional validation batches or change our process, specifications or third-party suppliers or contract manufacturers; and
- we may not be able to validate our manufacturing process to the satisfaction of the regulatory authorities, or they may not agree with our plan for potential retrospective validation.

If we fail to gain regulatory approval for RP103 for other indications or our other future drug product candidates, we will have to delay or terminate some or all of our research product development programs, and our business, results of operations and financial condition will be materially adversely affected.

We do not have internal manufacturing capabilities. Throughout most of 2015, we expect to continue to rely on a single source supplier for our active pharmaceutical ingredient, or API, and a single third-party manufacturer for the conversion to finished drug product. We also rely on third parties for the distribution and pharmaceutical services of PROCYSBI in the United States and the EEA. If we are unable to rely on these third parties, our revenue will be delayed or diminished and our business, results of operations and financial condition will be materially adversely affected.

We do not own or operate manufacturing facilities and currently lack the in-house capability to manufacture PROCYSBI or RP103. As a result, we currently contract with external contract manufacturing organizations, or CMOs, for commercial and clinical quantities of PROCYSBI and RP103 for the indications under development. We rely on a single source supplier for our cysteamine API. While we have procured additional manufacturing support with a second supplier for clinical supply of our finished drug product, for the majority of 2015, we will continue to rely on a single third-party manufacturer for supply of finished products until the second supplier can be validated and provide finished product. Our ability to obtain sufficient quantities of PROCYSBI and RP103 is constrained by limited supplies of raw materials and the limited capacity and output of these third parties. Furthermore, any reduction, delay or interruption in our supply of API from the single source supplier or of our supply of finished goods from our CMO, together with any additional required efforts to identify and qualify alternative sources of API supply, could result in significant additional operating costs, interruptions in product supply, delays in sales of PROCYSBI and delays in developing RP103 for additional indications. In addition, supply arrangements from alternative sources not currently under contract may not be available on acceptable economic terms, if at all.

The manufacture of pharmaceutical products requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products

often encounter difficulties in production, particularly in scaling up initial production to commercial requirements. Difficulties may arise related to internal processes, production costs and yields, quality control, including stability of the product and quality control testing, sourcing scarcities, resource constraints, equipment problems, shortages of qualified personnel, labor disputes, severe weather events, unstable political environments or financial difficulties at foreign facilities, as well as compliance with strictly enforced federal, state and foreign regulations. Manufacturers may breach their agreements with us or may terminate or decline to renew their agreements with us, whether due to our breach of the relevant agreements or based on their own business priorities. In addition, due to our small patient population, the manufacture of our drug may be given lower prioritization on the production line if manufacturing prioritization is decided by scale.

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Manufacturers and suppliers are subject to regulatory requirements covering, among other things, manufacturing, process controls, testing, quality control and record keeping and are subject to ongoing inspections by regulatory agencies. We have no direct control over the ability of our contract manufacturing parties to maintain adequate quality control, quality assurance and qualified personnel, and while final outputs are reviewed by our own internal quality control, we depend on our third-party supplier and manufacturers for compliance with the FDA's current cGMP requirements and other FDA requirements, the Drug Enforcement Administration's regulations and other rules and regulations prescribed by applicable non-U.S. regulatory authorities. If our contract manufacturing partners cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or other regulatory authorities, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities, and we may experience long delays and interruptions to our manufacturing supply and increased costs.

Pursuant to ongoing obligations from our NDA for PROCYSBI, we are required to collect and submit data to the FDA regularly regarding our currently observed clinical and commercial product profile and overall product safety assessment. While our current inventory falls within the specifications used during our clinical trials that support our NDA in the U.S. and marketing authorization application, or MAA, in Europe, we are currently evaluating our product specifications limit in light of new analytic data characterizing impurities and related substances and intend to submit requests to regulators in the U.S. and Europe for approval of revised PROCYSBI and RP103 specifications. We expect that there will continue to be intermittent delays in manufacturing or release of drug product as these issues are identified and addressed, and future release of drug product may depend on agreement of those and future specifications updates. If regulators reject our proposal to modify the specifications or require additional data to support the updated specifications, our ability to release drug product may be limited. Although we have stock of PROCYSBI on hand and believe we have enough PROCYSBI inventory to meet our near-term commercial needs in both the United States and the EEA, if there are material delays in the regulators' review and potential approval, we may experience an inventory shortfall, which would have a material adverse effect on sales of PROCYSBI.

If we or our third-party suppliers and manufacturers fail to comply with applicable regulatory requirements, we could experience significant delays or interruptions to our manufacturing supply that may result in the delay or suspension of our pre-clinical or clinical trials. In addition, a regulatory agency could issue warning letters or untitled letters, seek an injunction, impose civil or criminal penalties or monetary fines, suspend or withdraw regulatory approval, suspend any ongoing clinical trials, refuse to approve pending applications or supplements to applications, suspend or impose restrictions on operations, including costly new manufacturing requirements, seize or detain products or request that we initiate a product recall.

We also rely on a third-party logistics provider and specialty pharmacy to distribute PROCYSBI to patients in the United States and to pharmacies in the EEA and to collect from insurance companies and government agencies in the United States and from pharmacies in the EEA. Our ability to collect from a particular logistics provider is not only subject to such provider's credit worthiness but is also dependent, in part, on its ability to arrange for full reimbursement from third-party payors. The outsourcing of our distribution function is complex, and we may experience difficulties that could reduce, delay or stop shipments of PROCYSBI. If we encounter such distribution problems, and we are unable to quickly enter into a similar agreement with another specialty distributor on substantially similar terms, if at all, the distribution of PROCYSBI could become disrupted, resulting in reduced revenues, healthcare provider dissatisfaction and/or patient dissatisfaction, which may materially adversely affect our business, results of operations and financial condition.

If any of these events were to occur, our reputation would be harmed, revenues from sales of our products would be delayed or diminished and our business, results of operations and financial condition would be materially adversely affected.

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If serious adverse side effects become associated with PROCYSBI, our business, results of operations and financial condition will be materially adversely affected.

The prescribing information for PROCYSBI includes several warnings relating to observed adverse reactions of cysteamine bitartrate usage. The FDA may require products approved under Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act, or FDCA, to bear the same or similar warning statements as the reference product used in the approval. We expect to update adverse reactions listed in the prescribing information based on continued commercial use and additional clinical trials. If additional adverse reactions emerge, or if there is a pattern of severe or persistent previously observed side effects in the relevant patient populations, the FDA, the EMA or other regulatory agencies could modify or revoke our marketing approval, require us to modify our label or require us to suspend production, require a product recall, or we may choose to withdraw PROCYSBI from the market. Regulatory authorities could also require us to change the way the product is administered or modify the product in some other way, or they could require us to conduct additional clinical trials or costly post-marketing testing and surveillance to monitor the safety or efficacy of the product. If this were to occur, we may be unable to maintain marketing approval in our approved indications and/or obtain marketing approval in other indications. In addition, patients or their representatives may bring claims against us alleging serious adverse side effects or harm suffered as a result of use of PROCYSBI. Any such side effects or related claims could have a material adverse effect on our business, results of operations and financial condition. See also the risk factor titled “We may be subject to product liability claims.”

If we fail to demonstrate safety or efficacy in our preclinical studies or clinical trials or to keep to the terms of a product development program, our future business prospects for these drug product candidates will be materially adversely affected.

Clinical trials are very expensive, time consuming and difficult to design and implement. The outcome of clinical trials is uncertain, and results of earlier studies and trials may not be predictive of future trial results. Delays in the commencement or completion of clinical testing for RP103 or pre-clinical or clinical testing for any of our other product candidates could significantly affect our product development costs and business plan.

Preclinical studies involve testing in appropriate multiple non-human disease models to demonstrate efficacy and safety. Regulatory agencies evaluate these data carefully as part of their determination whether to authorize clinical testing in humans. If certain preclinical data reveal potential safety issues or if the results are inconsistent with an expectation of the drug product candidate’s efficacy in humans, the regulatory agencies may require additional testing before allowing human clinical trials. This additional testing will increase program expenses and extend timelines. There are many potential preclinical models to test for different disease states, and we could fail to choose the best preclinical model to determine proof of concept, safety and efficacy of our drug product candidates. We may decide to suspend further testing on our drug product candidates or technologies if, in the judgment of our management and advisors, the preclinical test results do not support further development.

Following successful preclinical testing, drug product candidates must be tested in a clinical development program to provide data on safety and efficacy in humans prior to becoming eligible for product approval and licensure by regulatory agencies. Success in preclinical testing and early clinical trials does not ensure that later clinical trials will be successful. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials. Clinical trials may also be delayed or repeated as a result of ambiguous or negative interim results or unforeseen complications in testing. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. The clinical trial process may fail to demonstrate with statistical significance that our drug product candidates are safe for humans and effective for indicated uses. This failure may cause us to abandon a drug product candidate and may delay development of other drug product candidates. Any delay in, or termination of, our preclinical testing or clinical trials will delay the filing of relevant marketing applications with regulatory agencies and, ultimately, our ability to commercialize our drug

product candidates and generate revenues from related products.

The rate of completion of any clinical trials will be dependent upon, among other factors, the rate of patient enrollment. Patient enrollment is a function of many factors, including the size of the patient population, the nature of the trial, the nature of the disease or medical condition being studied, the availability of alternative therapies and drugs, the proximity of patients to clinical sites and the eligibility criteria for the study. Delays in planned patient enrollment may result in increased costs and delays. In addition, because many of our clinical trials involve small patient populations, the results of these early clinical trials may not be indicative of future results.

Under the Prescription Drug User Fee Act, the FDA seeks to respond to NDAs within ten months of the filing date, but this timeframe is often extended. For example, a sponsor may seek FDA designation of a drug candidate as a “fast track product.” Fast track products are those products intended for the treatment of a serious or life-threatening disease or condition and which demonstrate the potential to address unmet medical needs for such disease or condition. If fast track designation is obtained, the FDA may initiate review of sections of an NDA before the application is complete. This “rolling review” is available if the applicant provides and the FDA approves a schedule for the remaining information. In addition, FDASIA established a new category of drugs referred to as “breakthrough therapies,” which are defined as drugs intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition where 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. In the future, we may request breakthrough designation or fast track designation from the FDA for our other drug product candidates, but we there can be no assurance that we will obtain such designations. Moreover, even if we obtain breakthrough designation or fast track designation from the FDA, the designations do not guarantee that the FDA will approve our NDA, that the development program or review timeline will ultimately be shorter than if we had not obtained the designations or that the FDA will not request additional information, including additional clinical studies, during its review.

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We do not know whether our investigational new drug, or IND, applications for future products or the protocols for any future clinical trials will be accepted by the FDA. We do not know if our clinical trials will begin or be completed on schedule or at all. Even if completed, we do not know if these trials will produce clinically meaningful results sufficient to support an application for marketing approval. The commencement and completion of our planned clinical trials could be substantially delayed or prevented by several factors, including:

- a limited number of, and competition for, suitable patients with particular types of disease for enrollment in clinical trials;
- delays or failures in obtaining regulatory clearance to commence a clinical trial;
- delays or failures in obtaining sufficient clinical materials;
- inability to design appropriate clinical trial protocols;
- delays or failures in reaching agreement on acceptable clinical trial agreement terms or clinical trial protocols with prospective sites;
- inability of our clinical research organizations, or CROs, or other third-party contractors to comply with all contractual requirements or to perform their services in a timely or acceptable manner;
- inability by us, our CROs or their employees to conduct the clinical trial in accordance with all applicable FDA, Drug Enforcement Administration or other regulatory requirements or our clinical protocols;
- lack of efficacy during, or other unfavorable results from, clinical trials or pre-clinical studies;
- discovery of serious or unexpected toxicities or side effects experienced by study participants or other unforeseen safety issues;
- failure of patients to complete the clinical trial, or inability or unwillingness of patients or medical investigators to follow our clinical trial protocols;
- inability to monitor patients adequately during or after treatment;
- regulatory action by the FDA or other regulatory authorities; and
- lack of adequate funding to continue the clinical trial, including the incurrence of any unforeseen costs.

In addition, changes in applicable regulatory requirements and guidance may occur, and we may need to amend clinical trial protocols to reflect these changes. Amendments may require us to resubmit our clinical trial protocols to Institutional Review Boards for reexamination, which may affect the costs, timing or successful completion of a clinical trial.

Sales of our products outside of the United States are also subject to foreign regulatory requirements governing clinical trials, manufacturing and marketing approvals. Even if the FDA and EC grant marketing approval for a product candidate, comparable regulatory authorities of foreign countries must also approve the manufacturing and marketing of our product candidates in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and greater than, those in the United States, including additional preclinical studies or clinical trials or manufacturing and control requirements. In many countries outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that country. In many cases, the price that we propose to charge for our products is also subject to approval by individual countries before we can launch our product candidates in those countries. Obtaining foreign regulatory approvals, complying with foreign regulatory requirements and gaining approved pricing and reimbursement could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. Further, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries. Regulatory approval in one country does not ensure approval in any other country, while a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory approval process in others.

Any delay in our preclinical or clinical programs or the failure to demonstrate safety or efficacy in our clinical trials would have a material adverse effect on our business, results of operations and financial condition.

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If we fail to maintain orphan drug or other regulatory exclusivity for PROCYSBI or to obtain and maintain exclusivity for our orphan drug product candidates, our competitors may sell products to treat the same conditions, possibly at lower prices, and our revenues will be significantly reduced.

PROCYSBI has received marketing approval from the FDA for the management of nephropathic cystinosis in adults and children six years and older and seven years of market exclusivity as an orphan drug in the United States. PROCYSBI has also received approval as an orphan medicinal product for the management of proven nephropathic cystinosis and 10 years of market exclusivity in the EEA. As part of our business strategy, we intend to develop RP103, and potentially other drugs, for additional therapeutic indications that may be eligible for FDA and EMA orphan drug designation.

Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, defined as a patient population of less 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 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. The company that first obtains FDA approval for a designated orphan drug for a given rare disease receives marketing exclusivity for use of that drug for the stated condition for a period of seven years, plus an additional six months if designated for a pediatric indication.

In the EU, the EMA's Committee for Orphan Medicinal Products 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 five in 10,000 persons in the EU and for which no satisfactory method of diagnosis, prevention or treatment has been authorized (or if the product would be a significant benefit to those affected). In addition, designation is granted for products intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition as well as when it is unlikely that sales of the drug in the EU would be sufficient to justify the necessary investment in developing the medicinal product without incentives. An EU orphan drug designation entitles a party to financial incentives such as reduced 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. An applicant must request orphan drug designation 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.

Even though we have been granted orphan drug designation in the United States and in the EU prior to the approval of RP103 for the potential treatment of HD, and even if we obtain orphan drug designation for our future drug product candidates, we may not fulfill the criteria for exclusivity, or we may not be the first to obtain marketing approval for any orphan indication. Further, even if we obtain orphan drug exclusivity for a particular product, that exclusivity may not effectively protect the product from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve a drug for the same condition if the FDA concludes that the later drug is safer, more effective or makes a major contribution to patient care. Orphan drug exclusive marketing rights may also be lost if the FDA later determines that the request for designation was materially defective, if a subsequent product is deemed clinically superior or if the manufacturer is unable to deliver sufficient quantities of the drug.

Because the extent and scope of patent protection for some of our drug products may be particularly limited, orphan drug designation is especially important for our eligible products and we plan to rely on the orphan exclusivity period to maintain a competitive position. However, if we do not obtain and/or maintain orphan drug exclusivity for RP103,

or if our drug products do not have strong patent protection, our competitors may sell the same drug to treat the same condition, possibly at lower prices, and our revenues will be reduced. Also, without strong patent protection, competitors may sell a generic version of our products upon the expiration of orphan exclusivity if our patent position is not upheld.

If our competitors succeed in developing products and technologies that are more effective than our own, or if scientific developments change our understanding of the potential scope and utility of our drug product candidates, then our technologies and future drug product candidates may be rendered less competitive.

We face significant competition from industry participants that are pursuing technologies similar to those that we are pursuing and are developing pharmaceutical products that are competitive with PROCYSBI or our drug product candidates. Many of the pharmaceutical companies in areas competitive with us have greater capital resources, larger overall research and development staff and facilities and a longer history in drug discovery, development, regulatory approval, manufacturing and marketing than we do. With these additional resources and experience, our competitors may be able to respond to rapid and significant technological changes in the biotechnology and pharmaceutical industries faster than we can.

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We expect that the technologies associated with biotechnology research and development will continue to develop rapidly. Our future success will depend in large part on our ability to maintain a competitive position with respect to these technologies. Rapid technological development, as well as new scientific developments, may result in our compounds, drug products, drug product candidates or processes becoming obsolete before we can recover any or all of the expenses incurred to develop them. For example, changes in our understanding of the appropriate population of patients who should be treated with a targeted therapy like those we are developing may limit the drug's market potential if it is subsequently demonstrated that only certain subsets of patients should be treated with the targeted therapy.

Because the target patient populations for PROCYSBI and some of our drug product candidates are small, we must achieve significant market share and obtain relatively high per-patient prices for our products to achieve meaningful gross margins.

PROCYSBI and our clinical development of RP103 target diseases with small patient populations, including cystinosis and Huntington's Disease, or HD, respectively. To successfully commercialize a drug product for these indications, we must identify patients and a targeted prescriber base for the drug product. Due to small patient populations, we believe that we would need to have significant market penetration to achieve meaningful revenues. In addition, the per-patient prices at which we sell PROCYSBI and RP103 for these indications will need to be relatively high in order for us to generate an appropriate return for the investment in these product development programs and to achieve meaningful gross margins. Patients who discontinue therapy or do not fill prescriptions are not easily replaced by new patients because of the limited patient population. There can be no assurance that we will successfully obtain or maintain sufficient market share or per-patient prices. Because the potential target populations are very small, even if we obtain significant market share for PROCYSBI and RP103, we may never achieve profitability despite obtaining such significant market share.

Our development strategy for RP103 depends upon the FDA's prior findings of safety and effectiveness of cysteamine bitartrate based on data not developed by us but upon which the FDA may rely in reviewing any future NDA.

The Hatch-Waxman Amendments added to the FDCA Section 505(b)(2), which permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference. Under this statutory provision, the FDA may rely, for purposes of approving an NDA, on safety and effectiveness data not developed by the filer of the NDA. We also plan to submit an NDA for RP103 for approval of other indications under Section 505(b)(2), and if we are able to submit those NDAs, they will rely, in part, on the FDA's previous findings of safety and effectiveness for cysteamine bitartrate. Even though we may be able to take advantage of Section 505(b)(2) to support potential U.S. approval for these additional product candidates, the FDA may require us to perform additional studies or measurements to support approval. In addition, the FDA's interpretation and use of Section 505(b)(2) has been controversial and has previously been challenged in court, though without a definitive ruling on the propriety of the FDA's approach. Future challenges, including a direct challenge to the approval of our products and product candidates, may be possible and, if successful, could limit or eliminate our ability to rely on the Section 505(b)(2) pathway for the approval of RP103 and our other product candidates. Such a result could require us to conduct additional testing and costly clinical trials, which could substantially delay or prevent the approval and launch of any future product candidates and would materially adversely affect our business, results of operation and financial condition.

If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate Program or other governmental pricing programs in the United States, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, results of operations and financial condition.

We participate in the Medicaid Drug Rebate Program, as administered by the Centers for Medicare & Medicaid Services, or CMS, and other federal and state government pricing programs in the United States, and we may participate in additional government pricing programs in the future. These programs generally require us to pay rebates or otherwise provide discounts to government payors in connection with drugs, including PROCYSBI, that are dispensed to beneficiaries of these programs. In some cases, such as with the Medicaid Drug Rebate Program, the rebates are based on pricing and rebate calculations that we report on a monthly and quarterly basis to the government agencies that administer the programs. Pricing and rebate calculations are complex, vary among products and programs, and are often subject to interpretation by governmental or regulatory agencies and the courts. The terms, scope and complexity of these government pricing programs change frequently. Responding to current and future changes may increase our costs and the complexity of compliance will be time consuming.

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In addition, the Office of Inspector General has recently increased its focus on the methodologies used by manufacturers to calculate average manufacturer price, or AMP, and best price, or BP, to assess manufacturer compliance with reporting requirements under the Medicaid Drug Rebate Program. We are liable for errors associated with our submission of pricing data and for any overcharging of government payors. For example, failure to submit monthly/quarterly AMP and BP data on a timely basis could result in a civil monetary penalty of $10,000 per day for each day the submission is late beyond the due date. Failure to make necessary disclosures and/or to identify overpayments could result in allegations against us under the Federal False Claims Act and other laws and regulations.

Any required refunds to the U.S. government or responding to a government investigation or enforcement action would be expensive and time consuming and could have a material adverse effect on our business, results of operations and financial condition. In the event that the CMS were to terminate our rebate agreement, no federal payments would be available under Medicaid or Medicare for our covered outpatient drugs.

Pressure from third-party payor coverage, reimbursement and pricing policies may impair our customers' ability to be reimbursed for PROCYSBI and our other future product candidates at adequate prices or on adequate terms, which may in turn materially adversely affect our business, results of operations and financial condition.

Market acceptance and sales of PROCYSBI and any product candidates that we may develop will depend in large part on third-party payor coverage and reimbursement policies and may be affected by future healthcare reform measures in the United States, the EEA countries and other key international markets. The continuing efforts of governmental and other third-party payors to contain, reduce or shift the costs of healthcare through various means, including an increased emphasis on managed care and attempts to limit or regulate the price of medicinal products and services, particularly for new and innovative products and therapies, may result in downward pressure on pricing, reimbursement and utilization, which may adversely affect our product sales and results of operations. Moreover, because private health insurers and other third-party payors often follow the coverage and reimbursement policies of government payors, including the Medicare and Medicaid programs, cost-containment measures under these programs play a particularly significant role in the reimbursement landscape. The government programs relevant to our products include, without limitation, the following:

- the Medicaid Drug Rebate Program, under which manufacturers must report pricing information and pay rebates in order for their drug products to be covered under state Medicaid programs;
- the Public Health Service's 340B Drug Pricing Program, under which manufacturers must offer discounts to certain healthcare organizations that care for underserved populations;
- the Department of Veterans Affairs' Federal Supply Schedule pricing program, under which manufacturers agree to offer drugs to certain governmental providers at reduced rates;
- the TRICARE Retail Pharmacy Program, under which manufacturers must agree to honor certain discounted prices, specifically Federal Ceiling Prices under the Veterans Health Care Act, as a condition for placement in the Department of Defense uniform formulary; and
- the Medicare Part D program, under which manufacturers contract with plan sponsors to offer certain outpatient drugs to Medicare beneficiaries.

In addition, in the United States, third-party payors often develop cost containment measures using policies that specifically target specialty products and high-cost drugs. For example, formulary placements may be less favorable for brand and higher-costing drugs, which may result in, among other things, greater out-of-pocket costs to patients. PROCYSBI often is subject to such measures, and similar future policies addressing such cost-containment measures may also affect PROCYSBI.

Further, third-party payors also are increasingly considering new metrics as the basis for reimbursement rates, such as average sales price, AMP or actual acquisition cost, and for cost-benefit analyses with comparable drugs. Although the changes to reimbursement methodologies are generally intended to limit payment increases, it is difficult to project

the impact of these and other alternative reimbursement methodologies on the willingness of payors to reimburse PROCYSBI and any product candidates that we may develop. To date, PROCYSBI generally has been covered and reimbursed in the United States and the select countries we have entered in Europe, but we do not know whether third-party payors will continue to cover and reimburse PROCYSBI in these markets or at the level PROCYSBI is currently covered, will reimburse PROCYSBI in other EEA countries or will reimburse RP103 and our future products until we enter into payor negotiations. If coverage and reimbursement are not available or are available only at limited levels, our business, results of operations and financial condition will be materially adversely affected.

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Legislative changes may increase the difficulty and cost for us to commercialize PROCYSBI or any other product candidate that we develop and affect the prices we may obtain.

In the United States, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that restrict or regulate post-approval activities. The changes may affect our ability to sell PROCYSBI or any other product candidate for which we obtain marketing approval at adequate prices.

In 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, which we refer to together as the "Affordable Care Act," was adopted. This law intends to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. The Affordable Care Act, among other things:

- increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program;
- revised the definition of AMP for reporting purposes, which could further increase the amount of rebates paid by manufacturers under the Medicaid Drug Rebate Program;
- extended the Medicaid Drug Rebate Program to beneficiaries enrolled in Medicaid managed care organizations;
- addressed 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 and for oral solid line extensions and reformulated drugs, which, depending on how the provision is interpreted and implemented, could increase our Medicaid rebate rate substantially;
- imposed a significant annual fee on companies that manufacture or import branded prescription drug products and
- established an annual non-deductible fee on entities that sell branded prescription drugs or biologics to specified government programs in the United States, beginning in 2011;
- expanded the 340B drug discount program (excluding orphan drugs), including the creation of new penalties for non-compliance; and
- included a 50% point-of-sale discount off negotiated prices on applicable brand-name drugs for Medicare Part D participants in the coverage gap, or "donut hole," as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D.

Other legislative and regulatory changes have also been proposed and adopted in the United States since the enactment of the Affordable Care Act. On August 2, 2011, the Budget Control Act of 2011 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. These automatic reductions included aggregate reductions of Medicare payments to providers of 2%. These reductions went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2024 unless additional Congressional action is taken.

In addition, legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. Increased scrutiny by the U.S. Congress of the FDA's approval process may subject us to more stringent product labeling and post-marketing testing and other requirements, and delays in feedback from the FDA may affect our ability to update or adjust our label in a timely manner in the interest of patient adherence and tolerability. We cannot predict whether other legislative changes will be adopted or how such changes would affect the pharmaceutical industry generally and the commercialization of PROCYSBI specifically.

Legislative changes regarding manufacturers' rebate obligations for new formulations of oral solid dosage form drugs under the Medicaid Drug Rebate Program, if applied to PROCYSBI, would have a material adverse effect on our business, results of operations and financial condition.

The Affordable Care Act created a new formula to determine the rebate amount owed by manufacturers of “line extension” drugs that would likely lead to higher rebates owed by such manufacturers under the Medicaid Drug Rebate Program. The Affordable Care Act defined a line extension drug to mean a new formulation of a drug, “such as an extended release formulation.” In April 2010, CMS stated that it would issue additional guidance to manufacturers and other stakeholders concerning line extensions of existing drugs. In 2012, in implementing the new law, CMS proposed a broad definition of a line extension drug to include any single source or innovator multiple source drug that is an oral solid dosage form approved by the FDA as a change to the initial brand name listed drug; a new formulation of a previously approved oral solid dosage form drug; a new combination of two or more oral solid dosage form drugs; or a new indication for an already marketed oral solid dosage form drug. In the proposed rule, orphan drugs were included as part of the definition of a line extension drug. Although CMS has not yet issued a final rule, CMS expects to finalize the rule in 2015. In the event that CMS finalizes the rule as currently proposed, PROCYSBI would likely be subject to the new rebate calculations under the Medicaid Drug Rebate Program, and, as a result, PROCYSBI sales to Medicaid beneficiaries would be reimbursed at cost and any profits from those sales would be eliminated. Approximately 20% of our current PROCYSBI sales are to Medicaid beneficiaries. Accordingly, the implementation of the proposed rules may have a material adverse effect on our business, results of operations and financial condition.

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We are subject, directly and indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, physician payment transparency laws, corrupt practices and bribery laws and health information privacy and security laws. Failure to comply with these laws may subject us to substantial penalties.

We do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payors. However, federal and state healthcare laws and regulations pertaining to fraud and abuse, physician payment transparency and privacy and security laws and regulations apply to us and our arrangements with healthcare providers, customers and other entities, including our marketing practices, educational programs and pricing policies. These laws 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, in exchange for or to induce either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under federal healthcare programs, such as the Medicare and Medicaid programs. A person or entity does not need to have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it to have committed a violation; in addition, 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;
- federal false claims 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 federal third-party payors that are false or fraudulent;
- the federal Civil Monetary Penalties law, which prohibits, among other things, offering or transferring remuneration to a federal healthcare beneficiary that a person knows or should know is likely to influence the beneficiary's decision to order or receive items or services reimbursable by the government from a particular provider or supplier;
- federal criminal laws that prohibit executing a scheme to defraud any federal healthcare benefit program or making false statements relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it to have committed a violation;
- the federal Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, which governs the conduct of certain electronic healthcare transactions and protects the security and privacy of protected health information;
- the federal Physician Payment Sunshine Act, which requires manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to CMS information related to payments or other "transfers of value" made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, and requires applicable manufacturers and group purchasing organizations to report annually to CMS ownership and investment interests held by the physicians described above and their immediate family members and payments or other "transfers of value" to such physician owners (manufacturers are required to submit reports to CMS by the 90th day of each calendar year);
- in the EEA, in various member states including France, the United Kingdom, the Netherlands, Italy and Spain, rules adopted by the legislator or self-regulatory industry bodies requiring the notification and/or publication of certain transfers of value from pharmaceutical companies to healthcare professionals (for example, France has recently adopted legislation (Law No. 2011-2012, or the "French Sunshine Act," and Decree no. 2013-414 which implements it) requiring pharmaceutical companies to disclose and publish agreements with or transfers of value to healthcare professionals);

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- the U.S. Foreign Corrupt Practices Act, or the FCPA, which prohibits corporations and individuals from paying, offering to pay or authorizing the payment of anything of value to any foreign government official, government staff member, political party or political candidate in an attempt to obtain or retain business or to otherwise influence a person working in an official capacity; the UK Bribery Act, which prohibits both domestic and international bribery, as well as bribery across both public and private sectors; and bribery provisions contained in the German Criminal Code, which, pursuant to draft legislation being prepared by the German government, may make the corruption and corruptibility of physicians in private practice and other healthcare professionals a criminal offense; and
- analogous state and foreign 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 payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the industry's voluntary compliance guidelines and the applicable 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.

The risk of our being found in violation of these laws is increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of interpretations. In addition, as we expand our development and commercialization activities outside of the United States, we will need to establish and expand business relationships with various third parties, such as independent contractors, distributors, vendors, advocacy groups and physicians, and we will interact more frequently with foreign officials, including regulatory authorities and physicians employed by state-run healthcare institutions who may be deemed to be foreign officials under the FCPA, the UK Bribery Act or similar laws of other countries that may govern our activities. Any interactions with any such parties or individuals where compensation is provided that are found to be in violation of such laws could result in significant civil and criminal penalties.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available under such laws, it is possible that some of our business activities, including our relationships with physicians and other healthcare providers, some of whom recommend, purchase and/or prescribe our products, could be subject to challenge under one or more of such laws. We are also exposed to the risk that our employees, independent contractors, principal investigators, consultants, vendors, distributors and CROs may engage in fraudulent or other illegal activity. While we have policies and procedures in place prohibiting such activity, misconduct by these parties could include, among other infractions or violations, intentional, reckless and/or negligent conduct or unauthorized activity that violates FDA regulations, including those laws that require the reporting of true, complete and accurate information to the FDA, manufacturing standards, federal and state healthcare fraud and abuse laws and regulations, laws that require the true, complete and accurate reporting of financial information or data or other commercial or regulatory laws or requirements. It is not always possible to identify and deter misconduct by our employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If our operations are found to violate any of the laws described above or any other laws and regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, the curtailment or restructuring of our operations, the exclusion from participation in federal and state healthcare programs and imprisonment, any of which could adversely affect our ability to market PROCYSBI, RP103 and other future drug candidates and materially adversely affect our business, results of operations and financial condition. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. See also the risk factor titled "If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate Program or other governmental pricing programs in the United States, we could be subject to additional reimbursement requirements, penalties, sanctions and fines which could have a material

adverse effect on our business, results of operations and financial condition."

Our reliance on third parties may result in delays in completing, or a failure to complete, preclinical testing, clinical trials or regulatory marketing submissions.

In the course of product development, we engage and collaborate with a variety of external organizations to perform services essential to drug product development. The organizations which perform services may include, but are not limited to: governmental agencies and university laboratories; other biotechnology and pharmaceutical companies; CMOs; CROs; distribution and supply (logistics) service organizations; contract testing organizations; consultants or consulting organizations with specialized knowledge based expertise; and intellectual property law firms.

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As a result of our engagement of these types of organizations to help us with our product development programs, many important aspects of our business are and will be out of our direct control. Nevertheless, we are responsible for ensuring that each of our product development programs complies with applicable regulatory requirements, and our reliance on these organizations does not relieve us of our regulatory responsibilities. If any such organizations we engage in the future fail to perform their obligations under our agreements with them or fail to perform in a satisfactory manner in compliance with applicable regulatory requirements, we may face delays in completing our development and commercialization processes for any of our drug product candidates and could be required to repeat testing or clinical trials, which would delay the regulatory approval process. Furthermore, any loss or delay in obtaining contracts with such entities may also delay the completion of our clinical trials, regulatory filings and the potential market approval of our drug product candidates.

Specifically, we have and will continue to rely on third parties, such as CROs and/or co-operative groups, to assist us in overseeing and monitoring clinical trials as well as to process the clinical results. Any failure of such third parties to perform or to meet the applicable standards will result in delays in or failures to complete trials. A failure by such third parties to observe the terms of a product development program for any particular product candidate or to complete the clinical trials for a product candidate in the anticipated time frame could materially adversely affect our business, results of operations and financial condition.

In addition, our dependence on collaborative arrangements with third parties subjects us to a number of risks that could harm our ability to develop and commercialize products:

- collaborative arrangements might not be available on terms which are reasonably favorable to us, or at all;
- disagreements with partners may result in delays in the development and marketing of products, termination of collaboration agreements or time consuming and expensive legal action;
- agreement terms may be difficult or costly to enforce;
- partners may not allocate sufficient funds or resources to the development, promotion or marketing of our product candidates, or may not perform their obligations as expected;
- partners may choose to develop, independently or with other companies, alternative products or treatments, including products or treatments which compete with ours;
- agreements with partners may expire or be terminated without renewal, or partners may breach agreements with us;
- business combinations or significant changes in a partner's business strategy or financial resources might adversely affect that partner's willingness or ability to fulfill its obligations to us; and
- the terms and conditions of the relevant agreements may no longer be suitable.

We cannot guarantee that we will be able to negotiate acceptable future collaboration agreements or that those currently in existence will make it possible for us to fulfill our objectives.

We depend on the support of key scientific and medical collaborators.

We must establish and maintain relationships with key opinion leaders, leading scientists and research institutions. We believe that such relationships are critical to establishing products as a standard of care for their approved indications. Although we have various medical and scientific advisors and research collaborations, there is no assurance that our advisors and our research collaborators will continue to work with us or that we will be able to attract additional advisors or collaborators. If we are not able to maintain existing or establish new clinical and scientific relationships to assist in our commercialization and research and development, we may not be able to establish our products as the standard of care or successfully develop our drug product candidates.

If we fail to maintain an effective system of internal controls, we may not be able to accurately report our financial results and prevent fraud.

The Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, requires, among other things, that we maintain effective internal control over financial reporting and disclosure controls and procedures. In particular, we must perform system and process evaluation and testing of our internal control over financial reporting to allow management to report on the effectiveness of our internal control over financial reporting, as required by Section 404 of the Sarbanes-Oxley Act. A report of our management is included under Item 9A. “Controls and Procedures” of this Annual Report on Form 10-K, and our auditors have provided an attestation report on our internal control over financial reporting in this annual report. During its evaluation of the effectiveness of internal control over financial reporting as of December 31, 2014, management identified a material weakness related to our inventory costing and overhead allocations for our commercial product PROCYSBI and determined that our review of our inventory costing and overhead allocations were not performed at a sufficiently detailed level to detect errors in our inventory and related accounts. With the oversight of management and our Audit Committee, we have initiated actions to address the root causes of the material weakness identified in 2014. There can be no assurance that such actions will be sufficient to remedy the material weakness identified or that additional material weaknesses or other control or significant deficiencies will not be identified in the future. If we continue to experience a material weakness in our internal controls or fail to maintain or implement required new or improved controls, such circumstances could cause us to fail to meet our periodic reporting obligations or result in material misstatements in our financial statements, or adversely affect the results of periodic management evaluations and annual auditor attestation reports. Each of the foregoing results could cause stockholders to lose confidence in our reported financial information and lead to a decline in our stock price. See Item 9A. “Controls and Procedures” for more information.

We may be subject to product liability claims.

The nature of our business exposes us to potential liability risks inherent in the testing (including through human trials), manufacturing and marketing of drugs. PROCYSBI and our drug product candidates could potentially harm people, and we may be subject to costly and damaging product liability claims regardless of actual harm. Many of the participants in our clinical trials and cystinosis patients who use PROCYSBI are already critically ill or suffering from chronic debilitating diseases. The waivers we obtain from participants in clinical trials may not be enforceable and may not protect us from liability or the costs of product liability litigation.

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We may not be able to avoid significant liability if any product liability claim is brought against us. Although we currently carry product liability insurance, it may not be sufficient to cover any claims. We may be unable to maintain product liability insurance in the future at satisfactory rates or in adequate amounts.

Regardless of the merits or eventual outcome, product liability claims may result in decreased demand for our product candidates, injury to our reputation, withdrawal of clinical trial participants and inability to continue clinical trials, costs to defend the related litigation, diversion of management's time, substantial monetary awards to trial participants, or patients, regulatory investigations, product recalls or withdrawals, labeling, marketing or promotional restrictions and loss of revenue, any of which may materially adversely affect our business, results or operations and financial condition.

Our success depends on our ability to manage our projected growth.

Our business strategy, including continued commercial sales of PROCYSBI in the United States and certain countries in the EEA, expansion of our commercial operations into other markets, the continuation of our clinical-stage programs and the in-license and acquisition of additional clinical-stage product candidates, will require us to retain existing and add required new qualified and experienced personnel in multiple functional areas over the next several years.

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 manage the expansion of our operations effectively, 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, including additional product candidates.

In addition, in connection with the commercial launch of PROCYSBI in the EEA, we have expanded our operations in Europe where we expect to continue to add personnel. We may encounter difficulties successfully managing remotely a substantially larger and internationally diverse organization and may encounter delays in commercialization if we are not successful in integrating our international operations. Challenges related to managing international operations may arise from staffing and managing foreign operations, reduced or varied protection for intellectual property rights in some countries, potential strain on our financial and managerial controls and reporting systems and procedures, diverse individual country regulatory and statutory laws, the costs of maintaining EEA presence, in-country legal entities and related tax structures, fluctuations in currency exchanges and political and economic instability, including wars, terrorism and political unrest, boycotts, curtailment of trade and other business restrictions.

If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate revenue could be reduced, and we may not be able to implement our business strategy.

Credit risks from customers outside the United States may materially adversely affect our business, results of operations and financial condition.

Sales of our products to government supported customers outside of the United States are likely to be subject to significant payment delays due to government funding and reimbursement practices, which will result in an increase in the length of time that we may have accounts receivable outstanding. In addition, many governments in Europe are facing significant liquidity crises. If government reimbursement for sales of PROCYSBI or any future products in EEA countries is delayed or becomes unavailable, we may not be able to collect on amounts payable to us in reasonable time frames from such customers, which would cause our capital requirements to increase and would materially adversely affect our business, results of operations and financial condition.

Macroeconomic conditions could materially adversely affect our business, results of operations and financial condition.

Various macroeconomic factors, such as changes in inflation, interest rates, foreign currency exchange rates and overall business and economic conditions and uncertainties, including those resulting from conditions in the global financial markets, could adversely affect our business, results of operations and financial condition. For example, if inflation or other factors were to significantly increase our business costs, it may not be feasible to increase the price of PROCYSBI or any future products due to reimbursement procedures and other pricing pressures.

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In the recent past, the global financial crisis caused financing to be unavailable in many cases or caused the cost of financing to significantly increase. Any similar disruption in the financial markets may increase uncertainty in the debt and equity markets, which may adversely affect our ability to access financing on favorable terms in the future. In addition, our suppliers, manufacturers and other third parties important to our business also may be negatively affected by such potential market dislocations and disruptions, and their businesses may be disrupted, which could materially adversely affect our business, results of operations and financial condition.

Our product sales in the United States could be reduced by imports from countries where our products are available at lower prices.

Our recognized product sales in the United States may be reduced if PROCYSBI is imported into the United States from lower-priced markets, whether legally or illegally. In the United States, prices for pharmaceuticals are generally higher than in the bordering nations of Canada and Mexico. There have been proposals to legalize the import of pharmaceuticals from outside the United States. If such legislation were enacted, our revenues could be reduced, and our business, results of operations and financial condition could be materially adversely affected.

Our international sales and operating expenses are subject to fluctuations in currency exchange rates.

A portion of our business is conducted in currencies other than our reporting currency, the U.S. dollar. We recognize foreign currency gains or losses arising from our operations in the period in which we incur those gains or losses. As a result, currency fluctuations between the U.S. dollar and the currencies in which we do business cause foreign currency translation gains and losses. Because of the number of currencies that may be involved as we enter new markets, the variability of currency exposures and the potential volatility of currency exchange rates, we may suffer significant foreign currency translation and transaction losses due to the effect of exchange rate fluctuations. We have not entered into derivative instruments to offset the impact of foreign exchange fluctuations. Given the volatility of exchange rates, there is no assurance that we will be able to effectively manage currency transaction and/or conversion risks.

We may engage in strategic transactions that could affect our liquidity, increase our expenses and present significant challenges in focus and energy to our management.

From time to time, we may consider strategic transactions, such as acquisitions of companies, asset purchases and out-licensing or in-licensing of intellectual property, products or technologies. Additional potential transactions that we may consider include a variety of business arrangements, including spin-offs, strategic partnerships, joint ventures, restructurings, divestitures, business combinations and investments. These transactions may entail numerous operational and financial risks, including exposure to unknown liabilities; disruption of our business and diversion of our management’s time and attention in order to develop acquired products or technologies or to conduct business in new markets; use of existing cash reserves, dilutive issuances of equity securities to replenish cash requirements or to directly pay for transactions, or incurrence of substantial debt to pay for acquisitions; higher-than-expected acquisition and integration costs; increases in near- and long-term expenditures; unexpected difficulties or shortcomings in the development or commercialization of acquired assets, products, or businesses; write-downs of assets or goodwill or impairment charges; increased amortization expenses; difficulty and cost in combining the operations and personnel of any future acquired businesses with our operations and personnel; impairment of relationships with key suppliers or customers of any acquired businesses due to changes in management and ownership; and inability to retain key employees of any acquired businesses.

Accordingly, although we cannot assure you that we will undertake or successfully complete any transactions of the nature described above, any transactions that we do complete may be subject to the foregoing or other risks and could have a material adverse effect on our business, results of operations and financial condition.

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Our business involves the use of hazardous materials, and we and our third-party manufacturers and suppliers must comply with environmental laws and regulations, which can be expensive and restrict how we do business.

Our research and development activities and those of our third-party manufacturers and suppliers involve the controlled storage, use and disposal of hazardous materials, including components of our product and 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 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. We do not currently carry biological or hazardous waste insurance coverage. 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.

Significant disruptions of information technology systems or breaches of data security could materially adversely affect our business, results of operations and financial condition.

We are increasingly dependent on information technology systems and infrastructure to operate our business. In the ordinary course of our business, we collect, store and transmit large amounts of confidential information, including intellectual property, proprietary business information and personal information. It is critical that we do so in a secure manner to maintain the confidentiality and integrity of such confidential information. We have also outsourced elements of our information technology infrastructure, and as a result a number of third-party vendors may or could have access to our confidential information. The size and complexity of our information technology systems, and those of third-party vendors with whom we contract, make such systems potentially vulnerable to breakdown, malicious intrusion, security breaches and other cyber-attacks. In addition, the prevalent use of mobile devices that access confidential information increases the risk of data security breaches, which could lead to the loss of confidential information, trade secrets or other intellectual property. The costs to us to eliminate or alleviate network security problems, bugs, viruses, worms, malicious software programs and security vulnerabilities could be significant, and while we have implemented security measures to protect our data security and information technology systems, our efforts to address these problems may not be successful, and these problems could result in unexpected interruptions, delays, cessation of service and other harm to our business. Despite the extensive measures we may take to secure data and our information technology systems, a determined hacker or other bad actor may still breach these security measures and our information technology systems. Moreover, if a computer security breach affects our systems or results in the unauthorized release of personally identifiable information, our reputation could be materially damaged. In addition, such a breach may require notification to governmental agencies, the media or individuals pursuant to various federal and state privacy and security laws, if applicable, including the Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Clinical Health Act of 2009, and its implementing rules and regulations, as well as regulations promulgated by the Federal Trade Commission and state breach notification laws. We would also be exposed to a risk of loss or litigation and potential liability, which could materially adversely affect our business, results of operations and financial condition.

Business disruptions from the occurrence of a catastrophic disaster could cause damage to our facilities and equipment or that of our third-party manufacturers or suppliers.

Our executive offices and laboratory facility are located in the San Francisco Bay Area near known earthquake fault zones and are vulnerable to significant damage from earthquakes. We and our contract manufacturers and source suppliers of raw materials and critical services are also vulnerable to damage from other types of disasters, including fires, storms and other extreme weather conditions, floods, water shortages, power losses, telecommunications failures, outbreaks of disease and similar events. If such a disaster were to occur, our ability to continue our operations, including commercial sales and product development programs, could be seriously, or potentially completely, impaired. The insurance we maintain may not be adequate to cover our losses resulting from disasters or other business interruptions, and we may not be able to maintain insurance in the future at satisfactory rates or in adequate amounts.

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Risks Related to Intellectual Property and Competition

If we are unable to protect adequately our proprietary technology, we may not be able to compete as effectively, and our business, results of operations and financial condition will be materially adversely affected.

Our success depends significantly on our ability to protect our proprietary technology from unauthorized use by third parties. We will be able to obtain such protection only to the extent our products are covered by valid and enforceable patents or trade secrets. Any non-confidential disclosure to or misappropriation by third parties of our confidential or proprietary information could enable competitors to quickly duplicate or surpass our technological achievements and erode our competitive position in the market. Where we elect to pursue patent protection on our proprietary technology, we file, prosecute and maintain patent applications covering certain aspects of our technology. Patent protection may not be available, however, for some of the drug product candidates we are developing. In addition, if we are required to spend significant time and money obtaining, maintaining and enforcing our patent rights, designing around patents held by others or obtaining licenses to third-party patents or other proprietary rights that cover aspects of our product candidates, our business, results of operations and financial condition will be materially adversely affected.

The patent application process, also known as patent prosecution, is expensive and time consuming. It is possible that we or our current licensors, or any future licensors or licensees, may not be able to prepare, file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner or identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. If our current licensors, or any future licensors or licensees, are not fully cooperative or disagree with us regarding any aspect of the prosecution, maintenance or enforcement of the patent rights covering our product candidates where they have decision-making rights on such matters, our preferred approach may not be followed and the scope, strength, duration or other aspects of such patent rights could be compromised.

In addition, our patents and applications or those of our licensors may not be prosecuted and enforced in a manner consistent with the best interests of our business. Defects in form in the preparation or filing of our patents or patent applications or those of our licensors may adversely affect proper priority claims, inventorship, claim scope or patent term adjustments. As a result, the patent rights we depend upon to protect our technology may be held invalid or unenforceable or may be limited in scope. Moreover, we cannot assure you that all of the patent applications that we own or license will issue as patents or that, if issued, the claims of such patents will have a scope that will be advantageous to us.

The rights granted to us under the issued patents, as well as those that may be granted on pending patent applications that we own or license, may not be of sufficient scope or strength to provide us with any meaningful protection or commercial advantage. In such case, competitors may be able to design around our patents or develop products that provide outcomes comparable to ours without infringing on our intellectual property rights. In addition, we may in the future be subject to claims by our former employees or consultants asserting an ownership right in our patents or patent applications as a result of the work they performed on our behalf. Although we generally require all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information or technology to assign or grant similar rights to us under their inventions arising while working for us, we cannot be certain that we have executed such agreements with all who may have contributed to our inventions and intellectual property, nor can we be certain that our agreements with such parties will not be breached.

If any of our patents or those of our licensors are challenged, invalidated or legally circumvented by third parties, and if we do not own other enforceable patents protecting our products, competitors could market products and use processes that are substantially similar to, or superior to, ours, and our business will suffer. Any of these outcomes could impair our ability to succeed against competition from third parties and materially adversely affect our business, results of operations and financial condition.

Our patents, even if issued, may not afford us the degree of protection we require to maintain a competitive advantage.

We own or license issued U.S. and foreign patents and pending U.S. and foreign patent applications related to certain of our drug product candidates and our other technologies. Evaluating the strength of patents covering our products candidates and other technologies in the biopharmaceutical field involves complex legal and scientific questions and can be highly uncertain. While we also rely on orphan drug exclusivity for PROCYSBI for commercial protection, the degree of patent protection we require may be unavailable or severely limited in some cases and may not adequately protect our products or permit us to gain or keep any competitive advantage. For example, the patent applications that we own or license may fail to result in issued patents in the United States or in other countries. Even if patents do issue on such patent applications, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. For example, U.S. patents can be challenged by any person before the new USPTO Patent Trial and Appeals Board at any time within the one-year period following that person’s receipt of an allegation of infringement of the patents. Patents granted by the European Patent Office may be similarly opposed by any person within nine months from the publication of the grant. Similar proceedings are available in other jurisdictions, and in the United States, Europe and other jurisdictions, third parties can raise questions of validity with a patent office even before a patent has granted.

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Even if they are unchallenged, our patents and patent applications, if granted, may not adequately protect our product candidates or technology or prevent others from designing around our patent claims. For example, a third party may develop a competitive product that provides therapeutic benefits similar to one or more of our product candidates but that has a different composition that falls outside the scope of our patent protection. If the breadth or strength of protection provided by the patents and patent applications we own or license covering our product candidates is successfully challenged, then our ability to commercialize such product candidates could be adversely affected, and we may face unexpected competition that may materially adversely affect our business, results of operations and financial condition.

In addition, competitors may interfere with our success in obtaining and maintaining patent protection for our product candidates and technologies in a variety of ways. Competitors may claim that they invented the claimed invention prior to us or our licensors or may file patent applications before we or our licensors do. Competitors may also claim that we are infringing on their patents and that we therefore cannot develop or commercialize our product candidates or practice our technology. Competitors may also challenge our patents, if issued, by showing the patent examiner that the invention claimed was not original, was not novel or was obvious. In litigation, a competitor could claim that our patents, if granted, are not valid for a number of reasons. If a court agrees, we would lose some or all of our rights to the challenged patents.

Furthermore, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after it is filed. Various extensions may be available; however, the life of a patent, and the protection it affords, is limited. Without adequate and continuing patent protection for our product candidates and technologies, we may be open to competition from generic versions of such products and competitive versions of our technologies.

If we do not obtain, or if we lose, adequate patent protection for our product candidates, and if we do not have other regulatory exclusivity for such product candidates as described under the risk factor titled “If we fail to maintain orphan drug or other regulatory exclusivity for PROCYSBI or to obtain and maintain exclusivity for our orphan drug product candidates, our competitors may sell products to treat the same conditions, possibly at lower prices, and our revenues will be significantly reduced,” others may develop and commercialize products that are the same as, or similar to, our product candidates, which would adversely affect our business, results of operations and financial condition.

We may in the future become involved in lawsuits to defend against third-party allegations of infringement or to protect or enforce our intellectual property, which could be expensive, time consuming and unsuccessful and have a material adverse effect on our business, results of operations and financial condition.

The drug product and biopharmaceutical industry has been characterized by frequent and extensive intellectual property litigation. Our competitors or other third-party patent holders may assert that our products are covered by their patents. Although we believe we have adequate defenses available if faced with any allegations that we infringe third-party patents, we cannot be certain that we do not infringe on those patents or that we will not infringe on patents granted in the future. Furthermore, because patent applications can take many years to issue and may be confidential for 18 months or more after filing, and because pending patent claims can be revised before issuance, there may be applications now pending which may later result in issued patents that may be infringed by the manufacture, use or sale of our products. If a patent holder believes our drug product infringes on its patent, the patent holder may sue us even if we have received patent protection for our technology. Moreover, we may face patent infringement claims from non-practicing entities that have no relevant product revenue and against whom our own patent portfolio may thus have no deterrent effect. If our products are found to infringe, we could be prevented from manufacturing or marketing those products.

In addition, competitors may infringe our patents or misappropriate or otherwise violate our intellectual property rights. To stop any such infringement or unauthorized use, litigation may be necessary. If we or one of our licensors or licensees were to initiate legal proceedings against a third party to enforce a patent, the defendant could counterclaim

that our patent 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 for patent issuance, including lack of novelty, obviousness or non-enablement. Patents may be unenforceable if someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution. The outcomes of proceedings involving assertions of invalidity and unenforceability are unpredictable. Furthermore, prior art that would render our patents invalid may exist. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability of our patents covering one of our product candidates or technologies, we would lose at least part, and perhaps all, of the patent protection on such product candidates or technologies. Such a loss of patent protection would materially adversely affect our business, results of operations and financial condition, particularly if we do not have other regulatory protection. Moreover, our competitors could counterclaim in any suit to enforce our patents that we infringe their intellectual property.

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Third parties may initiate legal proceedings against us to challenge the validity or scope of our intellectual property rights or may allege an ownership right in our patents resulting from their past employment or consultancy with us. Many of our current and potential competitors have the ability to dedicate substantially greater resources to defend their intellectual property rights than we can. Accordingly, despite our efforts, we may not be able to prevent third parties from claiming an ownership interest in or infringing upon or misappropriating our intellectual property. Competing products may also be sold in other countries in which our patent coverage might not exist or be as strong. If we lose a foreign patent lawsuit alleging our infringement of a competitor's patents, we could be prevented from marketing our product candidates in one or more foreign countries.

Litigation related to infringement or misappropriation of intellectual property rights, with or without merit, is unpredictable, is generally expensive and time consuming and can divert management's attention from our core business. If we do not prevail in any litigation in which we are alleged to have infringed or misappropriated intellectual property rights, a court could require us to pay substantial damages, treble damages and attorneys' fees and could prohibit us from using technologies essential to our product candidates, any of which would have a material adverse effect on our business, results of operations and financial condition. If patents asserted against us are upheld as valid and enforceable and we are found to infringe them, we could be prevented from selling our product candidates or technologies unless we can obtain licenses to use the technology or ideas covered by such patents. We do not know whether any necessary licenses would be available to us on satisfactory terms, if at all. If we cannot obtain such licenses, we could be forced to design around the infringed patents at additional cost or to abandon the infringing product candidate or technology altogether. 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 market price of our common stock. As a result, our ability to grow our business and compete in the market may be harmed.

We may also support and collaborate in research conducted by government organizations, hospitals, universities or other educational institutions. These research partners may be unwilling to grant us any exclusive rights to technology or product candidates derived from these collaborations. If we do not obtain required licenses or rights, we could encounter delays in our product development efforts while we attempt to design around other patents or even be prohibited from developing, manufacturing or selling drug product candidates requiring these licenses. There is also a risk that disputes may arise as to the rights to technology or drug product candidates developed in collaboration with other parties. Any such disputes may cause our competitive position to be adversely affected and may materially adversely affect our business, results of operations and financial condition.

Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. In addition, periodic maintenance fees on issued patents often must be paid to the USPTO and foreign patent agencies over the lifetime of the patent. While an unintentional lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we fail to maintain the patents and patent applications covering our product candidates or technologies, we may not be able to prevent a competitor from marketing products that are the same as or similar to our products, which would have a material adverse effect on our business, results of operations

and financial condition, particularly if we do not have other regulatory protection for our products.

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

Filing, prosecuting and defending patents on our product candidates and technologies in all countries throughout the world would be prohibitively expensive. The requirements for patentability may differ in certain countries, particularly in developing countries. Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws. In addition, laws of some countries outside of the United States do not afford intellectual property protection to the same extent as the laws of the United States. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property rights. This could make it difficult for us to stop the infringement of our patents or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States. In addition, competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection, if our ability to enforce our patents to stop infringing activities is inadequate. 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. See also the risk factor titled “Our success depends on our ability to manage our projected growth.”

Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and resources from other aspects of our business. Furthermore, while we intend to protect our intellectual property rights in major markets for our products, there can be no assurance that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our products. In addition, our efforts to protect our intellectual property rights in such countries may be inadequate.

Changes to the patent law in the United States and other jurisdictions 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 our having valid and enforceable intellectual property rights, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve both technological and legal complexity and is therefore costly, time consuming and inherently uncertain. Recent patent reform legislation in the United States and other countries, including the Leahy-Smith America Invents Act, or Leahy-Smith Act, signed into law on September 16, 2011, could increase those uncertainties and costs. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art and provide more efficient and cost-effective avenues for competitors to challenge the validity of patents. In addition, the Leahy-Smith Act has transformed the U.S. patent system into a “first to file” system. The first-to-file provisions, however, only became effective on March 16, 2013. Accordingly, it is not yet clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could make it more difficult to obtain patent protection for our inventions and 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 materially adversely affect our business, financial condition and results of operations.

The U.S. Supreme Court has ruled on several patent cases in recent years, narrowing the scope of patent protection available in certain circumstances and weakening the rights of patent owners in certain situations. In addition, there have been recent proposals for additional changes to the patent laws of the United States and other countries that, if adopted, could affect our ability to obtain patent protection for our proprietary technology or our ability to enforce our proprietary technology. Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in

unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

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If we are limited in our ability to utilize acquired or licensed technologies, or if we lose our rights to critical in-licensed technology, we may be unable to successfully develop, out-license, market and sell our products, which could prevent or delay new product introductions.

We have acquired and licensed certain proprietary technologies and plan to further license and acquire various patents and proprietary technologies owned by other parties. The agreements in place are critical to our product development programs. For example, most of our patent portfolio pertaining to PROCYSBI and RP103 for cystinosis and other therapeutic indications has been licensed from academic institutions. Our license agreements with these institutions include termination clauses that permit the licensor to terminate our license under certain circumstances, including if we materially breach our obligations under the applicable agreement. If one or more of our licenses is terminated, we would have no further right to use or exploit the patents, know-how and other intellectual property rights licensed to us under the agreement, which could adversely affect our ability to market PROCYSBI or continue our development programs of RP103 in other clinical indications.

Our business strategy depends on the successful development of licensed and acquired technologies into commercial products. Therefore, any limitations on our ability to utilize these technologies may impair our ability to develop, out-license or market and sell our product candidates, could delay new product introductions and could adversely affect our reputation, any of which could have a material adverse effect on our business, results of operations and financial condition.

If we are unable to protect the confidentiality of our trade secrets, our competitive position may be harmed, and our business, results of operations and financial condition will be materially adversely affected.

In addition to patent protection, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. Our trade secrets may not be adequately protected, however. We have taken steps to protect our trade secrets and proprietary information, including entering into confidentiality agreements and intellectual property assignment agreements with our employees, consultants, advisors and corporate and educational institution partners. Nevertheless, such agreements may not be enforceable or may not provide meaningful protection for our trade secrets or other proprietary information in the event of unauthorized use or disclosure, whether willful or unintentional, or other breaches of the agreements, and we may not be able to prevent such unauthorized disclosure. Monitoring unauthorized disclosure is difficult, and we do not know whether the steps we have taken to prevent such disclosure are, or will be, adequate. In addition, we may not be able to obtain adequate remedies for any such breaches. Enforcing a claim that someone illegally obtained and is using our trade secrets, like patent litigation, is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States may be less willing to protect trade secrets. Our competitors may independently develop equivalent knowledge, methods and know-how. Competitors could purchase our products and attempt to replicate some or all of the competitive advantages we derive from our development efforts, willfully infringe or misappropriate our intellectual property rights, design around our protected technology or develop their own competitive technologies that fall outside of our intellectual property rights. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us.

We may be subject to damages resulting from claims that we or our employees have wrongfully used or disclosed alleged trade secrets of our competitors or are in breach of non-competition or non-solicitation agreements with our competitors.

We could in the future be subject to claims that we or our employees have inadvertently or otherwise used or disclosed alleged trade secrets or other proprietary information of former employers or competitors. Although we try to ensure that our employees and consultants do not use the intellectual property, proprietary information, know-how or trade secrets of others in their work for us, we may in the future be subject to claims that we caused an employee to

breach the terms of his or her non-competition or non-solicitation agreement or that we or these individuals have, inadvertently or otherwise, used or disclosed the alleged trade secrets or other proprietary information of a former employer or competitor in breach of their obligations to that employer or competitor. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and could be a distraction to management. If our defenses to these claims fail, in addition to requiring us to pay monetary damages, a court could prohibit us from using technologies or features that are essential to our products, if such technologies or features are found to incorporate or be derived from the trade secrets or other proprietary information of the former employers. An inability to incorporate such technologies or features would have a material adverse effect on our business, and may prevent us from successfully commercializing our products. In addition, we may lose the right to practice valuable intellectual property rights or personnel as a result of such claims. Moreover, any such litigation or the threat thereof may adversely affect our ability to hire employees or contract with independent sales representatives. A loss of key personnel or their work product could hamper or prevent our ability to commercialize our products. Any of these events, or a combination thereof, could have a material adverse effect on our business, results of operations and financial condition.

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Risks Related to Our Financial Position and Capital Requirements

Our commercial operations and clinical development programs will require substantial future funding which will affect our operational and financial condition.

Our commercial sales programs for PROCYSBI and any future approved products and our product development programs will require substantial additional capital, arising from costs incurred to:

- conduct research, preclinical testing and human studies and clinical trials; develop and submit regulatory submissions for marketing approvals;
- develop and submit regulatory submissions for marketing approvals;
- establish or contract for pilot scale and commercial scale manufacturing processes and facilities;
- obtain adequate reimbursement for our products;
- market and distribute PROCYSBI and any future approved products; and
- establish, develop and maintain quality control, manufacturing, regulatory, medical, distribution, marketing, sales, finance and administrative capabilities to support these programs.

We base our outlook regarding the need for funds on many uncertain variables. Such uncertainties include the success of our commercial sales of PROCYSBI in the United States, the EEA and any additional markets; the success of our efforts to commercialize any future approved products; the scope and results of our research initiatives, preclinical testing and human clinical trials; regulatory approvals; the timing of events outside our direct control, such as competing technological and market developments, negotiations with third-party payors and potential strategic partners; and other factors. In addition, certain product programs may require collaborative agreements with corporate partners with greater financial and organizational resources than we have. Such agreements may require substantial time to complete and may not be available in the time frame desired or with acceptable financial terms, if at all. Any of these factors may significantly change the timing and amount of our cash requirements as they determine such one-time events as the receipt or payment of milestone-based and other payments.

If we fail to raise additional financing when needed, we may have to delay or terminate some or all of our research and development programs, scale back our operations and/or reduce our commercial finance and administrative expenses to sustainable levels, which would have a material adverse effect on our business, results of operating and financial condition.

While we believe that, based upon our projected PROCYSBI sales and planned operations, our cash and cash equivalents as of December 31, 2014 of approximately $150 million will be sufficient to meet our projected operational requirements and obligations through 2016, we will need to sell equity or debt securities to raise additional funds to support, among other things, our development and commercialization programs. The sale of additional equity securities or convertible debt securities will result in additional dilution to our stockholders, and newly issued securities may have rights, preferences and privileges senior to those of holders of our common stock. Additional financing may not be available on a timely basis, in amounts or on terms satisfactory to us, or at all. We may be unable to raise additional capital due to a variety of factors, including our financial condition, the status of our research and development programs, the status of regulatory reviews for marketing approvals, the status of our commercialization activities, sales of PROCYSBI in existing and additional markets and the general condition of the financial markets. If we fail to raise additional financing when needed, we may have to delay, partner, or terminate some or all of our research and development programs, scale back our operations and/or reduce our commercial expenses. If such actions are required, our business, results of operations and financial condition will be adversely affected, and the market value of our common stock may significantly decline.

Our loan agreement with HC Royalty and outstanding convertible senior notes contain a number of restrictive covenants and other provisions, which, if violated, could result in the acceleration of the payment terms of our

outstanding indebtedness, which in turn could have a material adverse effect on our business, results of operations and financial condition.

In December 2012, we entered into a loan agreement with HealthCare Royalty Partners II, L.P., or HC Royalty, as lender, which we refer to as the HC Royalty Loan Agreement. Under the HC Royalty Loan Agreement, we agreed to borrow $50.0 million in two $25.0 million tranches. We drew down the first tranche in the amount of $25.0 million in December 2012 and the second tranche of $25.0 million in May 2013 when we achieved the milestone of U.S. approval of PROCYSBI. In July 2014, we entered into an amendment and restatement of the original HC Royalty Loan Agreement and borrowed from HC Royalty a third, $10.0 million tranche under the loan facility. Also in July 2014, we issued $60.0 million aggregate principal amount of 8.0% convertible senior notes due 2019 to HC Royalty and other purchasers.

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The HC Royalty Loan Agreement includes a number of affirmative and negative covenants, including requirements to use commercially reasonable efforts to exploit PROCYSBI and RP103 in specific markets and to comply with applicable laws, and additional restrictions on mergers, sales of assets, the incurrence of liens, the incurrence of additional indebtedness and transactions with our affiliates, among other requirements. The convertible senior notes also include a number of affirmative and negative covenants, including our obligation to offer to repurchase the notes upon a change of control of our company, limitations on the incurrence of additional indebtedness, registration rights for the holders of the notes and other requirements.

The performance of our obligations under the HC Royalty Loan Agreement is secured by our grant of a security interest to HC Royalty in substantially all of our assets and the assets of our domestic subsidiaries and a pledge of stock of certain of our domestic subsidiaries. Our failure to comply with the terms of the HC Royalty Loan Agreement, the convertible senior notes and related documents could result in an event of default. A change of control of our company, an uncured material adverse effect on our company and certain other specified events could also constitute an event of default under the agreements. In the event of an event of default that is not cured or waived, the payment of all of our indebtedness to HC Royalty and interest thereon and the repayment of the convertible senior notes could accelerate. Under the terms of the security agreement, an event of default could also enable the lender to take possession of, foreclose on, sell, assign or grant a license to use our pledged collateral and to assign and transfer the pledged stock of certain of our subsidiaries. An event of default, a material adverse effect or a change of control would also trigger a prepayment penalty under the HC Royalty Loan Agreement, which would require us to pay a substantially higher amount due than the current balance of our loan.

Any of the events described above, or a combination thereof, could have a material adverse effect on our financial condition and results of operations.

Our cash flows and capital resources may be insufficient to make required payments on our indebtedness.

The required payments of principal and interest on our indebtedness under the HC Royalty Loan Agreement and convertible senior notes may require a substantial portion, or all, of our available cash to be dedicated to the service of these debt obligations. Both the HC Royalty Loan Agreement and the convertible senior notes bear interest at an annual fixed rate of 8.0%. The HC Royalty Loan Agreement also bears a synthetic royalty based on our net revenues from PROCYSBI and other future-approved products in a calendar year. This royalty and the interest under the HC Royalty Loan Agreement and the convertible senior notes are payable quarterly. Principal payments under the HC Royalty Loan Agreement will become due beginning in June 2015. The convertible senior notes will mature on August 1, 2019, unless earlier converted, redeemed or repurchased.

There can be no assurance that our business will generate sufficient cash flow or that we will have capital resources in an amount sufficient to enable us to pay our indebtedness to HC Royalty or the holders of the convertible senior notes. Our debt obligations may also limit our flexibility to plan for or react to changes in our business and industry and place us at a competitive disadvantage compared to competitors with superior financial resources including less debt. If our cash flows and capital resources are insufficient to fund these debt service obligations, we may be forced to reduce or delay product development, sales and marketing and capital and other expenditures. We may also be forced to restructure our indebtedness or raise additional capital through the issuance of equity or debt instruments, and there can be no assurance that we will be able to refinance any of our indebtedness or raise additional capital on a timely basis, in sufficient amounts, on satisfactory terms or at all. The terms of the HC Royalty Loan Agreement and convertible senior notes may also limit our ability to pursue any of these financing alternatives, and these alternatives nonetheless may not enable us to meet our scheduled debt service obligations.

Failure to meet our debt service obligations may result in an event of default under the HC Royalty Loan Agreement, which would permit the lender to accelerate the payment of all of our indebtedness to HC Royalty and interest thereon. An event of default could also enable the lender to take possession of, foreclose on, sell, assign or grant a

license to use our pledged collateral and to assign and transfer the pledged stock of certain of our subsidiaries. An event of default, a material adverse effect or a change of control would also trigger a prepayment penalty under the HC Royalty Loan Agreement, which would require us to pay a substantially higher amount than the current balance of our loan.

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Failure to meet our debt service obligations may also result in an event of default under the convertible senior notes, which would permit the holders to accelerate the payment of the outstanding principal amount of the notes and interest thereon and require us to pay a repayment premium and higher interest. A change of control would also trigger an obligation to repurchase the convertible senior notes.

Any of the events described above, or a combination thereof, could have a material adverse effect on our business, financial condition and results of operations.

Our ability to use our net operating losses to offset future taxable income may be subject to certain limitations.

In general, under Section 382 of the Internal Revenue Code of 1986, as amended, a corporation that undergoes an "ownership change" is subject to limitations on its ability to utilize its pre-change net operating loss carryforwards to offset future taxable income. Our existing net operating loss carryforwards may be subject to limitations arising from previous ownership changes, and if we undergo an ownership change in the future, our ability to utilize our net operating loss carryforwards could be further limited by Section 382. Future changes in our stock ownership, some of which are outside of our control, could result in an ownership change. Furthermore, we may be unable to use a substantial part of our net operating loss carryforwards if we do not attain profitability in an amount sufficient to utilize such losses.

Risks Related to Our Common Stock

Our stock price has been volatile and may continue to be volatile in the future, and our stockholders may not be able to resell shares of our common stock at or above the prices that they paid. The trading volume in our common stock may be relatively small.

Our common stock is quoted on the NASDAQ Global Market. The trading price of our common stock has been and may continue to be volatile. During the 52-week period ended February 20, 2015, our average daily trading volume was approximately 813,664 shares and the closing sales price per share of our common stock on the NASDAQ Global Market ranged from $7.51 to $17.41. Our operating performance, both financial and in the development of approved products, significantly affects the market price of our common stock. A number of factors may affect the market price of our common stock, including:

- the success of our testing and clinical trials and those of others with products similar or related to our products;
- announcements regarding regulatory approvals or approved label indications and patient populations or changes or delays in the regulatory review process;
- unexpected difficulties in commercialization or lower than expected sales;
- lower than expected pricing and reimbursement levels, or no reimbursement at all, for our products in various markets;
- actions taken by regulatory agencies with respect to our clinical trials, manufacturing supply chain or sales and marketing activities;
- changes in our relationships with manufacturers, suppliers or collaborators, or our inability to supply enough product to meet demand;
- announcements of new products or innovations by us or our competitors and announcements concerning our competitors or our industry in general;
- our ability to obtain additional funding;
- changes or developments in applicable laws or regulations;
- any intellectual property infringement actions in which we may become involved;
- sales and profitability;
- announcements of significant acquisitions, strategic partnerships, joint ventures, or capital commitments by us, our strategic collaboration partners or our competitors;

- our ability to manage our projected growth;
- actual or anticipated fluctuations in our results of operations;
- changes in financial estimates or recommendations by securities analysts or their ceasing to publish research or reports about our business;
- the trading volume of our common stock;
- general economic and market conditions and overall fluctuations in the U.S. equity markets;

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- the appeal and current level of investor interest in the biotechnology/biopharmaceutical capital market sector and in companies in general with business, research strategies and product development pipelines which are similar to us; and
- the loss of any of our key scientific or management personnel.

For planning purposes, we estimate the timing of the accomplishment of various scientific, clinical, regulatory, market launch and commercialization goals, which we sometimes refer to as milestones. These milestones include the completion of reimbursement and pricing negotiations and commercial launches in additional territories, commencement or completion of scientific studies and clinical trials and the submission of regulatory filings. We also prepare estimates of future financial results for planning and budget purposes. From time to time, we may publicly announce the estimated timing of some of these milestones and provide guidance regarding financial results and other metrics. All of these projections will be based on a variety of assumptions. The actual timing of these milestones and actual financial results can vary dramatically compared to our estimates for a number of reasons, including those set forth above, in many cases for reasons beyond our control. If we do not meet the milestones, financial guidance or other expectations as publicly announced or as projected by various security analysts who follow our company, our stockholders or potential stockholders may lose confidence in our ability to meet overall objectives and our financial planning capabilities, and as a result, the market price of our common stock may decline.

In addition, the NASDAQ Global Market has, from time to time, experienced extreme price and trading volume fluctuations. The market prices of securities of pharmaceutical, biotechnology and other life sciences companies in a comparable stage to ours historically have been particularly volatile, and trading volume in such securities and our common stock has often been relatively small. Moreover, the stock markets in general have experienced substantial volatility that has often been unrelated or disproportionate to the operating performance of individual companies. During certain periods, the favor of certain industry segments, such as the biotechnology segment, may also be volatile. These changes may affect in particular the market price of our common stock and the stock prices of companies such as ours that do not have conventional measures of financial and business health such as sales, earnings, profitability and related measures. These broad market fluctuations, during which our industry and companies at our stage may experience a stronger degree of market sensitivity, will adversely affect the market price of our common stock. In the past, following periods of volatility in the market resulting in substantial declines in the market price of a company’s securities, stockholders have often instituted class action securities litigation against those companies. Such litigation can result in substantial costs and diversion of management attention and resources, which could significantly harm our and reputation and materially adversely affect our business, financial condition and results of operations.

Future sales or issuances of our common stock or other securities in the public market, including shares issuable upon conversion of our convertible senior notes, or the perception of such future sales or issuances, could lead to a decline in the market price of our common stock.

Any issuance of shares of our common stock or other securities, including for the purposes of raising capital to fund our operations, acquisitions and the expansion of our business, will have a dilutive effect on our existing stockholders. In addition, any issuance or the perceived market risk associated with any possible issuance could cause the market price of our common stock to decline. Subsequent sales of our common stock in the open market, exercises of our currently outstanding stock options, conversion of our convertible senior notes and the subsequent sale of the shares acquired thereunder or any other issuance by us of shares of our common stock or other securities could also have an adverse effect on the market price of our common stock. If the market price of our common stock declines, it will be more difficult for us to raise additional capital, or we may be unable to raise additional capital at all.

In addition, we have in the past and may in the future grant rights to some of our stockholders that require us to register the resale of shares or our common stock on behalf of these stockholders and/or to facilitate offerings of shares of our common stock held by these stockholders, including in connection with potential future acquisitions of

additional products, product candidates or companies. If holders of such registration rights sell a large number of shares of our common stock, the sale could cause the market price of our common stock to decline. We have also filed registration statements to register the sale of our shares of our common stock reserved for issuance under our equity incentive plans and our employee stock purchase plan and intend to file additional registration statements to register any shares added to the reserves under these plans.

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In July 2014, we issued $60.0 million aggregate principal amount of 8.0% convertible senior notes due 2019. The convertible senior notes are convertible at the option of the holder at an initial conversion rate of approximately 57.14 shares of common stock per $1,000 principal amount of convertible senior notes, which is equivalent to an initial conversion price of $17.50, and is subject to adjustment upon certain events and conditions. In addition, we may redeem for cash or require holders to convert the convertible senior notes into shares of common stock if the price of the common stock is at or above 175% of the applicable conversion price over a period of 30 consecutive trading days. The note purchase agreement governing the convertible senior notes provides the holders with registration rights for the shares issued upon conversion of their convertible senior notes subject to certain conditions, and we have filed a registration statement to register the resale of the shares of common stock issuable upon conversion of the convertible senior notes. We may be required to pay increased interest on the convertible senior notes if we do not comply with the registration rights provisions of the note purchase agreement. A substantial number of shares of our common stock are reserved for issuance upon conversion of the convertible senior notes. The issuance of shares of our common stock upon conversion of the convertible senior notes would dilute the ownership interest of our common stockholders and may materially adversely affect the market price of our common stock and impair our ability to raise capital through the sale of additional equity securities.

In connection with other collaborations, joint ventures, license agreements or future financings that we may enter into in the future, we may issue additional shares of common stock or other equity securities, and the value of the securities issued may be substantial and create additional dilution to our common stockholders.

Because we do not intend to pay any cash dividends on our common stock, investors will benefit from an investment in our common stock only if it appreciates in value. Investors seeking dividend income should not purchase shares of our common stock.

We have not declared or paid any cash dividends on our common stock since our inception. We anticipate that we will retain our earnings to support our operations and to finance the growth and development of our business and do not expect to pay cash dividends in the foreseeable future. Our loan agreement with HC Royalty prohibits us from paying cash dividends. As a result, the success of an investment in our common stock will depend upon any future appreciation in the market price of our common stock. There can be no guarantee that the market price our common stock will appreciate or that it will not depreciate. Investors seeking dividend income should not invest in our common stock.

Anti-takeover provisions under Delaware law, in our stockholder rights plan and in our certificate of incorporation and bylaws, as amended, may prevent or complicate attempts by stockholders to change the board of directors or current management and could make a third-party acquisition of us difficult.

Our certificate of incorporation and bylaws, as amended, contain provisions that could significantly reduce the value of our shares to a potential acquirer or delay or prevent changes in control or changes in our management without the consent of our board of directors. The provisions in our charter documents include the following:

- the right of our board of directors to elect a director to fill a vacancy created by the expansion of the board of directors or the resignation, death or removal of a director, which prevents stockholders from being able to fill vacancies on our board of directors;
- the required approval of at least 66 2/3% of the shares entitled to vote to remove a director without cause;
- the ability of our board of directors to authorize the issuance of shares of preferred stock and to determine the price and other terms of those shares, including preferences, dividend rights and voting rights, which may be superior to those of the common stock, without stockholder approval, which could be used to significantly dilute the ownership of a hostile acquiror;
- the ability of our board of directors to alter our bylaws without obtaining stockholder approval;

the required approval of at least 66 2/3% of the shares entitled to vote at an election of directors to adopt, amend or repeal our bylaws;

- a prohibition on stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders;
- the requirement that a special meeting of stockholders may be called only by the chairman of the board of directors, the chief executive officer or the board of directors, which may delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors; and
- advance notice procedures that stockholders must comply with in order to nominate candidates to our board of directors or to propose matters to be acted upon at a stockholders' meeting, which may discourage or deter a potential acquiror from conducting a solicitation of proxies to elect the acquiror's own slate of directors or otherwise attempting to obtain control of us.

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We are also subject to the anti-takeover provisions contained in Section 203 of the Delaware General Corporation Law. Under Section 203, a corporation may not, in general, engage in a business combination with any holder of 15% or more of its capital stock unless the holder has held the stock for three years or, among other exceptions, the board of directors has approved the transaction.

We are also party to a stockholder rights plan, also referred to as a “poison pill,” which is intended to deter a hostile takeover of us by making such proposed acquisition more expensive for and less desirable to the potential acquirer.

Our board of directors may use the provisions described above to prevent changes in the management and control of our company. These provisions could limit the price that investors might be willing to pay in the future for shares of our common stock. These provisions would apply even if we were to receive an offer that some stockholders may consider beneficial. Also, under applicable Delaware law, our board of directors may adopt additional anti-takeover measures in the future.

Provisions of the note purchase agreement governing our convertible senior notes may discourage a takeover, which could cause the market price of our common stock to decline.

The repurchase rights and related repurchase premium provided in our convertible senior notes triggered by the occurrence of a change of control may discourage, delay or prevent a third party from acquiring us, even if doing so would benefit our stockholders. In turn, this could cause the market price of our common stock to decline.

ITEM 1B: UNRESOLVED STAFF COMMENTS

None.

ITEM 2: PROPERTIES

We lease 52,319 square feet of office and laboratory space as our headquarters in Novato, California. This space is situated in two adjacent facilities.

In addition, we lease small office spaces in Paris, France and Frankfurt, Germany; and in Utrecht, Netherlands as our European sales, marketing and administrative headquarters. We believe that our current facilities are sufficient to meet our present requirements.

ITEM 3: LEGAL PROCEEDINGS

From time to time we are involved in litigation arising out of claims in the normal course of business. We are not aware of any material pending legal proceedings against us, nor are we involved as a plaintiff in any material pending legal proceedings.

ITEM 4: MINE SAFETY DISCLOSURES

Not applicable.

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PART II

ITEM 5: MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Our common stock trades on the NASDAQ Global Market under the symbol “RPTP.” As of February 20, 2015, there were 69,144,463 shares of our common stock outstanding. There is no public trading market for our warrants. The closing price for our common stock on February 20, 2015 was $9.89 per share.

The following table sets forth the range of high and low sales prices of our common stock for the quarterly periods indicated, as reported by NASDAQ.

	High	Low
Fiscal Year Ended December 31, 2014:		
First Quarter (January 1 – March 31, 2014)	$17.72	$9.38
Second Quarter (April 1 – June 30, 2014)	12.19	7.12
Third Quarter (July 1 – September 30, 2014)	12.20	8.00
Fourth Quarter (October 1 – December 31, 2014)	11.10	7.85
Fiscal Year Ended December 31, 2013:		
First Quarter (January 1 – March 31, 2013)	6.28	4.71
Second Quarter (April 1 – June 30, 2013)	10.47	5.40
Third Quarter (July 1 – September 30, 2013)	15.00	9.26
Fourth Quarter (October 1 – December 31, 2013)	15.29	11.09

Holders of Record

As of February 20, 2015, there were approximately 118 holders of record of our common stock. In addition, as of February 20, 2015 there were warrants held by six holders of record to acquire up to, in the aggregate, 334,764 shares of our common stock.

Dividends

We have not declared or paid any cash dividends on our common stock since our inception. We anticipate that we will retain our earnings to support our operations and to finance the growth and development of our business and do not expect to pay cash dividends in the foreseeable future. In addition, our loan agreement with HC Royalty prohibits us from paying cash dividends.

Securities Authorized for Issuance under Equity Compensation Plans

Information regarding securities authorized for issuance under equity compensation plans is incorporated by reference into the information in Part III, Item 12 of this Annual Report on Form 10 K.

Recent Sales of Unregistered Securities

We did not issue any unregistered equity securities during the year ended December 31, 2014.

Purchase of Equity Securities and Affiliated Purchasers

We did not repurchase any shares of our common stock during the three months ended December 31, 2014.

Performance Graph

The following is not deemed "filed" with the Securities and Exchange Commission and is not to be incorporated by reference into any filing we make under the Securities Act of 1933, as amended, whether made before or after the date hereof and irrespective of any general incorporation by reference language in such filing.

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The following graph shows the value of an investment of $100 on September 30, 2009 (the date of our 2009 Merger) in our common stock, the NASDAQ Composite Index (U.S.), and the NASDAQ Biotechnology Index. All values assume reinvestment of the pretax value of dividends paid by companies included in these indices and are calculated as of August 31, 2010, 2011, 2012, for the four months ended December 31, 2012 and as of the years ended December 31, 2013 and 2014. The comparisons shown in the graph are based upon historical data and we caution that the stock price performance shown in the graph is not indicative of, nor intended to forecast, the potential future performance of our stock.

	September 30, 2009	August 31, 2010	2011	2012	Four Months Ended December 31, 2012	December 31, 2013	2014
Raptor Pharmaceutical Corp.	100.00	90.30	143.33	150.61	177.27	394.55	318.79
NASDAQ U.S. Composite Index	100.00	99.60	121.53	144.50	142.27	196.78	223.14
NASDAQ Biotechnology Index	100.00	96.73	119.13	168.82	170.41	282.22	378.45

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ITEM 6: SELECTED FINANCIAL DATA

The following table shows selected historical consolidated financial and operating information for, and as of the end of, each of the periods indicated and should be read in conjunction with the information in the sections titled, "Management's Discussion and Analysis of Financial Condition and Results of Operation" and "Business" and our consolidated financial statements and the corresponding notes to those consolidated financial statements included elsewhere in this Annual Report on Form 10-K. The following tables set forth our consolidated statements of operations and comprehensive loss data for the years ended December 31, 2014 and 2013, the four months ended December 31, 2012 and the fiscal years ended August 31, 2012, 2011 and 2010, and select consolidated balance sheet data as of December 31, 2014 2013 and 2012 and as of August 31, 2012, 2011 and 2010.

	For the Year Ended December 31,		For the Four Months Ended December	For the Year Ended August 31,		
(In millions, except per share data)[1]	2014	2013	31, 2012	2012	2011	2010
Statements of operations and comprehensive loss:						
Revenues	$69.5	$16.9	$ -	$-	$-	$-
Cost of sales	9.4	1.7	-	-	-	-
Gross profit	60.1	15.2	-	-	-	-
Operating expenses:						
Research and development	43.5	29.2	8.9	21.4	14.8	9.3
Selling, general and administrative	56.7	37.9	9.0	14.7	6.2	3.7
Total operating expenses	100.1	67.1	17.9	36.1	21.0	13.0
Loss from operations	(40.1)	(51.9)	(17.9)	(36.1)	(21.0)	(13.0)
Interest income	0.1	0.1	0.2	0.3	0.1	-
Interest expense	(14.0)	(6.8)	(0.1)	-	-	-
Foreign currency transaction gain	0.3	-	0.1	0.2	-	-
(Loss) gain on short-term investments	-	(0.1)	(0.1)	0.2	-	-
Adjustment to fair value of common stock warrants	(1.1)	(10.7)	(1.5)	(3.2)	(16.3)	(5.9)
Other income	2.3	-	-	-	-	-
Net loss before provision for income taxes	(52.5)	(69.4)	(19.3)	(38.6)	(37.2)	(18.9)
Provision for income taxes	(0.1)	-	-	-	-	-
Net Loss	$(52.5)	$(69.4)	$ (19.3)	$(38.6)	$(37.2)	$(18.9)
Other comprehensive gain (loss):						
Foreign currency translation gain (loss)	0.3	(0.3)	(0.1)	(0.1)	-	-
Comprehensive Loss	$(52.2)	$(69.7)	$ (19.4)	$(38.7)	$(37.2)	$(18.9)
Net loss per share:						
Basic and diluted	$(0.83)	$(1.20)	$ (0.37)	$(0.80)	$(1.15)	$(0.85)
Weighted-average shares outstanding	63.2	57.9	51.7	48.1	32.3	22.2

(In millions)	December 31,		August 31,	

Balance Sheet:	2014	2013	2012	2012	2011	2010
Cash, cash equivalents and short-term investments	$149.6	$83.1	$ 58.4	$38.9	$15.2	$17.0
Working capital (deficit)	142.5	66.2	37.0	(20.6)	(11.0)	(0.3)
Total assets	189.1	108.7	68.1	48.3	22.6	24.4
Common stock warrant liability	0.7	7.1	16.4	17.3	23.6	15.8
Note payable	60.0	50.0	25.0	-	-	-
Convertible notes	60.0	-	-	-	-	-
Total liabilities	140.1	80.2	48.2	21.6	26.7	17.6
Accumulated deficit	(257.9)	(205.4)	(135.9)	(116.6)	(78.0)	(40.8)
Total stockholders' equity (deficit)	48.9	28.6	19.9	26.7	(4.1)	6.8

(1) Certain totals may not foot due to rounding

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ITEM 7: MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

Overview

You should read the following discussion in conjunction with our consolidated financial statements as of December 31, 2014, and the notes to such consolidated financial statements included elsewhere in this Annual Report on Form 10-K. The "Management's Discussion and Analysis of Financial Condition and Results of Operations" section contains forward-looking statements. Please see "Forward-Looking Statements" for a discussion of the uncertainties, risks and assumptions associated with these statements. Our actual results and the timing of certain events could differ materially from those anticipated in these forward-looking statements as a result of certain factors, including those discussed below and elsewhere in this Annual Report on Form 10-K, particularly under the heading "Risk Factors," and in other documents we file with the SEC.

Change in Fiscal Year End

On December 4, 2012, our board of directors approved a change in our fiscal year end from August 31 to December 31. The change became effective at the end of the four months ended December 31, 2012. All references to "fiscal years" or "years" prior to this change refer to the twelve-month fiscal period covering September 1 through August 31, and each year after December 31, 2012, the fiscal year covers January 1 through December 31.

Plan of Operation and Overview

We are a biopharmaceutical company focused on developing and commercializing life-altering therapeutics that treat debilitating and often fatal diseases.

Our product, PROCYSBI® (cysteamine bitartrate) delayed-release capsules, or PROCYSBI, received marketing approval from the U.S. Food and Drug Administration, or FDA, in April 2013 for the management of nephropathic cystinosis in adults and children six years and older. In Europe, PROCYSBI gastro-resistant hard capsules of cysteamine (as mercaptamine bitartrate), received a marketing authorization in September 2013 from the European Commission, or EC, as an orphan medicinal product for the management of proven nephropathic cystinosis in the European Union, or EU. The EU marketing authorization allows us to commercialize PROCYSBI in the 28 Member States of the EU plus Norway, Liechtenstein and Iceland (which are not EU Member States but are part of the European Economic Area, or EEA). PROCYSBI received seven and ten years of market exclusivity due to its designation as an orphan drug in the United States and the EU, respectively. We achieved first commercial sales of PROCYSBI in the United States in June 2013 and in the EU, specifically in Germany, in April 2014.

Clinical Development Programs

Our three active clinical development programs utilize RP103, which contains the same active pharmaceutical ingredient as PROCYSBI, cysteamine bitartrate. RP103 is our proprietary extended and delayed-release formulation capsule containing enteric coated microbeads of cysteamine bitartrate. Cysteamine bitartrate was approved in the United States in 1994 and the EU in 1997 as an orally available immediate-release powder in a capsule for the management of cystinosis. We have an exclusive worldwide license from the University of California, San Diego (“UCSD”), to delayed-release cysteamine bitartrate, which is the basis for our proprietary formulation of cysteamine. We currently have product candidates in clinical development designed to potentially treat Huntington's disease (“HD”), non-alcoholic steatohepatitis (“NASH”), and Leigh syndrome and other mitochondrial disorders.

Our other clinical-stage product candidate is Convivia®, our proprietary oral formulation of 4-methylpyrazole, for the potential management of acetaldehyde toxicity due to alcohol consumption by individuals with aldehyde

dehydrogenase, or ALDH2, deficiency, an inherited metabolic disorder.

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Preclinical Product Candidates

Our preclinical programs, for which we may seek development partners in the future, include our cysteamine dioxygenase, or ADO, program and our HepTide® program, for the potential treatment of hepatocellular carcinoma and other cancers susceptible to induced lysosomal storage.

Future Activities

Over the next fiscal year, our efforts will be focused on increasing sales of PROCYSBI in the U.S. and Europe; launching PROCYSBI in other countries in the EU; filing a New Drug Submission, or NDS, for cysteamine bitartrate delayed-release capsules with Health Canada in 2015; conducting a clinical trial to evaluate PROCYSBI in cystinosis patients that are cysteamine-naïve, as well as other supporting trials in underdeveloped markets; developing select global markets with significant numbers of known cystinosis patients; screening for undiagnosed and unidentified adult nephropathic cystinosis patients; supporting regulatory pathways and/or clinical trials of RP103 for the potential treatment of HD, pediatric NASH, Leigh syndrome and mitochondrial disorders; enhancing and expanding our product manufacturing capabilities; preparing for potential clinical studies of RP103 in new therapeutic indications; supporting our novel preclinical programs; and identifying promising products and drug development candidates for in-licensing.

We plan to seek additional business development partners in Asia for our Convivia product candidate. We may also develop new preclinical, clinical and or commercial opportunities, including proprietary molecules discovered in-house and in-licensed and acquired technologies.

Application of Critical Accounting Policies

Our consolidated financial statements and accompanying notes are prepared in accordance with generally accepted accounting principles used in the United States. Preparing financial statements requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenue and expenses. These estimates and assumptions are affected by management's application of accounting policies. We believe that understanding the basis and nature of the estimates and assumptions involved with the following aspects of our consolidated financial statements is critical to an understanding of our consolidated financial position and results of operations.

Many of the following critical accounting policies require us to make significant judgments and estimates in the preparation of our consolidated financial statements.

Revenue Recognition and Accounts Receivable

We recognize revenue in accordance with the Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC 605, Revenue Recognition, when the following criteria have been met: persuasive evidence of an arrangement exists; delivery has occurred and risk of loss has passed; the seller's price to the buyer is fixed or determinable and collectability is reasonably assured. We determine that persuasive evidence of an arrangement exists based on written contracts that define the terms of the arrangements. Pursuant to the contract terms, we determine when title to products and associated risk of loss has passed onto the customer. We assess whether the fee is fixed or determinable based on the payment terms associated with the transaction and whether the sales price is subject to refund or adjustment. We assess collectability based primarily on the customer's payment history and creditworthiness.

PROCYSBI is currently available for U.S. distribution from our U.S. specialty pharmacy partner, the Accredo Health Group, Inc. (“Accredo”) which is currently our only U.S. customer and ships directly to patients. Our commercial

launch in the E.U. commenced in April 2014, with the Almac Group, Ltd. as our distributor. PROCYSBI is not available in U.S. retail pharmacies. Prior to the third quarter of 2014, revenue was recognized in the United States once the product had been shipped by the specialty pharmacy to patients because we had not yet been able to reasonably estimate the third-party payor mix and resulting rebates due to the lack of sufficient historical data. Beginning July 2014, we were able to reasonably estimate and determine sales allowances; therefore we began recognizing PROCYSBI revenue at the point of sale to the specialty pharmacy, which resulted in the one-time non-recurring recognition of an additional $4.4 million in net revenues during the quarter ended September 30, 2014. Revenue is currently recognized in the EU once confirmed orders from the pharmacies have been shipped and invoiced for payment by our distributor on our behalf.

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We record revenue net of expected discounts, distributor fees, and rebates, including government rebates such as Medicare and Medicaid in the United States. Allowances are recorded as a reduction of revenue at the time product sales are recognized. Allowances for government rebates and discounts are established based on the actual payor and payor mix information, which is known in the United States at the time of shipment to the distributor and in Germany at the time of shipment to the pharmacy, and the government-mandated discount rates applicable to government-funded programs. The allowances are adjusted to reflect known changes in the factors that may impact such allowances in the quarter the changes are known.

Trade accounts receivable are recorded net of product sales allowances for prompt-payment discounts and chargebacks. Estimates for chargebacks and prompt-payment discounts are based on contractual terms and our expectations regarding the utilization rates.

Inventories and Cost of Sales

Inventories are stated at the lower of cost or market price, with cost determined on a first-in, first-out basis. Inventories are reviewed periodically to identify slow-moving inventory based on sales activity, both projected and historical, as well as product shelf-life. Prior to the approval of PROCYSBI by the FDA on April 30, 2013 and in Europe, prior to EC approval on September 6, 2013, we recorded the purchase of raw materials and the manufacturing costs relating to PROCYSBI as research and development expense. Subsequent to FDA and EC approval, we began capitalizing these costs and manufacturing overhead as commercial inventory. Upon launching PROCYSBI in mid-June 2013 in the United States and April 2014 in the EU, we began recognizing cost of sales. Cost of sales includes the cost of inventory sold or reserved; manufacturing, manufacturing overhead and supply chain costs; product shipping and handling costs; and amortization of licensing approval milestone payments and licensing royalties payable to UCSD.

We capitalize inventory produced in preparation for product launches and expanded access programs when positive results have been obtained for the clinical trials that we believe are necessary to support regulatory approval and we have determined it is probable that these capitalized costs will provide some future economic benefit in excess of capitalized costs. For these inventories, we also consider the expected approval date in assessing realizability. To the extent that inventory is expected to expire prior to being sold, we will write down the value of inventory. If actual results differ from those estimates, additional inventory write-offs may be required.

Note Payable

Note payable consists of loan agreements with HC Royalty as lender, totaling $60 million. In July 2014, we modified our original December 2012 loan agreement with HC Royalty as lender, under which we borrowed $50 million in two $25 million tranches received in December 2012 and May 2013, to provide for an additional $10 million in term loan funding. The interest rate was revised to an annual fixed rate of 8.0%, compared to the original interest rate of 10.75%. The loan also contains a synthetic royalty component based on net product revenues, including PROCYSBI, in a calendar year, and such royalty is payable quarterly. The variable royalty rate under the amended and restated loan agreement has been revised to 8.0% on the first $50 million of revenue and 2.0% on revenue in excess of $50 million. The first loan principal payment of $3 million per quarter is due in June 2015. All term loans under the amended and restated loan agreement mature on March 31, 2020. The loan and our obligation to make payments thereunder shall terminate immediately when all payments received by HC Royalty equal $120 million.

Prior to July 1 2014, the loan bore interest at an annual fixed rate of 10.75% of outstanding principal and included a synthetic royalty component based on net product sales, including PROCYSBI, in a calendar year. With respect to the first $25 million tranche, for each calendar year, the loan bore a royalty rate of 6.25% of the first $25 million of product net revenues, 3.0% of product net revenues for such calendar year in excess of $25 million and up to $50 million, and 1.0% of product net revenues for such calendar year in excess of $50 million, payable quarterly. With

respect to the second $25 million tranche, for each calendar year, the loan bore a royalty rate of 6.0% of the first $25 million of product net revenues for such calendar year, 3.0% of product net revenues for such calendar year in excess of $25 million and up to $50 million, and 1.0% of product net revenues for such calendar year in excess of $50 million, payable quarterly.

The fixed and royalty interest are recognized as interest expense as incurred. The revenue related royalty interest may lead to significant fluctuations in interest expense from period to period.

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Convertible Notes

In July 2014, we sold $60 million aggregate principal amount of 8.0% convertible senior notes due 2019 to HC Royalty and other purchasers. These convertible notes require quarterly interest distributions at a fixed coupon rate equal of 8.0% until maturity or conversion, which will be no later than August 1, 2019. The convertible senior notes are convertible at the option of the holder at a conversion rate of 57.14 common shares per $1,000 principal amount of convertible senior notes at issuance (equivalent to a conversion price of $17.50 per common share), subject to adjustment in certain events. In addition, the convertible senior notes will automatically convert into shares of common stock if the price of the common stock is at or above 175% of the applicable conversion price over a 30 consecutive day period. Upon conversion of these convertible senior notes by a holder, the holder will receive shares of our common stock. The fixed interest payments are recognized as interest expense as incurred.

Impairment of Goodwill and Intangible Assets

Goodwill represents the excess of the purchase price over the fair value of tangible and identified intangible net assets of businesses acquired. Goodwill is not amortized, but is evaluated for impairment on an annual basis or more often when impairment indicators are present. We have one reporting unit. Therefore, our consolidated net assets, including existing goodwill and other intangible assets, are considered to be the carrying value of the reporting unit. If the carrying value of the reporting unit is in excess of its fair value, an impairment may exist, and we must perform the second step of the analysis, in which the implied fair value of the goodwill is compared to its carrying value to determine the impairment charge, if any. If the estimated fair value of the reporting unit exceeds the carrying value of the reporting unit, goodwill is not impaired and no further analysis is required. We performed our goodwill impairment test as of December 31, 2014 and noted no impairment.

We make judgments about the recoverability of purchased intangible assets with finite lives whenever events or changes in circumstances indicate that impairment may exist. Recoverability of purchased intangible assets with finite lives is measured by comparing the carrying amount of the asset to the future undiscounted cash flows the asset is expected to generate. Impairment, if any, is measured as the amount by which the carrying value exceeds the fair value of the impaired asset.

Assumptions and estimates about future values and remaining useful lives of our purchased intangible assets are complex and subjective. They can be affected by a variety of factors, including external factors such as industry and economic trends and internal factors such as changes in our business strategy and our internal forecasts.

Common Stock Warrant Liabilities

The common stock warrants we issued in connection with certain fiscal year 2010 equity financings contain conditional obligations that may require us to transfer cash to settle the warrants upon the occurrence of certain fundamental transactions. Therefore, we have classified the warrants as liabilities. We re-measure the liability at the end of every reporting period with the change in value reported in our consolidated statements of operations. At the exercise date, the fair values of these warrants are re-measured and reclassified to equity.

We use the Black-Scholes option pricing model as our method of valuation for warrants that are subject to warrant liability accounting. The determination of the fair value as of the reporting date is affected by our stock price as well as assumptions regarding a number of highly complex and subjective variables. These variables include, but are not limited to, expected stock price volatility over the term of the security and risk-free interest rate. In addition, the Black-Scholes option pricing model requires the input of an expected life for the securities for which we have estimated based upon the stage of our development. The fair value of the warrant liability is revalued each balance sheet date utilizing Black-Scholes valuation model computations with the decrease or increase in fair value being reported in the statement of operations as other income or expense, respectively. The primary factors affecting the fair

value of the warrant liability are our stock price and volatility. In addition, the Black-Scholes option pricing model requires the input of highly subjective assumptions, and other reasonable assumptions could provide differing results.

We reported a net loss of $52.5 million for the year ended December 31, 2014. If our December 31, 2014 closing stock price had been 10% lower, our net loss would have been approximately $0.1 million lower. If our December 31, 2014 closing stock price had been 10% higher, our net loss would have been approximately $0.1 million higher.

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If our December 31, 2014 volatility assumption had been 10% lower, our net loss would have been approximately the same. If our December 31, 2014 volatility assumption had been 10% higher, our net loss would have been approximately the same.

We reported a net loss of $69.4 million for the year ended December 31, 2013. If our December 31, 2013 closing stock price had been 10% lower, our net loss would have been approximately $0.9 million lower. If our December 31, 2013 closing stock price had been 10% higher, our net loss would have been approximately $0.9 million higher

If our December 31, 2013 volatility assumption had been 10% lower, our net loss would have been approximately $0.1 million lower. If our December 31, 2013 volatility assumption had been 10% higher, our net loss would have been approximately $0.1 million higher.

Stock-Based Compensation

Determining the fair value of share-based awards at the grant date requires judgment, including estimating future stock price volatility and employee stock option exercise behavior.

We based our Black-Scholes inputs on the following factors: the expected life of six years was based upon our assessment of the ten-year term of the stock options issued, along with the fact that we have been a commercial company since June 2013 and as a result, more option holders have been exercising stock options; the risk-free interest rate was based on current constant maturity treasury bill rates for six years; the volatility was based on a combination of the actual annualized volatility of our common stock price as quoted on NASDAQ since the closing of our 2009 Merger on September 30, 2009 and of annualized volatility of peer companies; the forfeiture rate was based on our assessment of our historical employee turnover; and the dividend rate was based on our current decision to not pay dividends on our stock at our current corporate stage of development. If actual results differ significantly from these estimates, stock-based compensation expense and results of operations could be materially impacted. Prior to 2014, we utilized an expected life of five years. See Note 11 of our consolidated financial statements for a further discussion of our accounting for stock-based compensation.

Income Taxes

Income taxes are recorded under the liability method, under which deferred tax assets and liabilities are determined based on the difference between the financial statement and tax bases of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to affect taxable income. Valuation allowances are established when necessary to reduce deferred tax assets to the amount expected to be realized. Based on the weight of available evidence, including cumulative losses since inception and expected future losses, we have determined that it is more likely than not that the deferred tax asset amount will not be realized and therefore a full valuation allowance has been provided on our net deferred tax assets. We intend to maintain the valuation allowance until sufficient positive evidence exists to support the reversal of the valuation allowance. Any decision to reverse part or all of the valuation allowance would be based on our estimate of future profitability.

We identify uncertain tax positions and record or disclose any resulting potential tax liability based upon whether the position is more likely than not sustainable upon examination. We consider proposed assessments by tax authorities, changes in facts and circumstances, issuance of new regulations or new case law and negotiations between tax authorities of different countries concerning our transfer prices or intellectual property transfers. As of December 31, 2014, we had identified no uncertain tax positions.

We file U.S. Federal, California, various other state and other income tax returns and various foreign country income tax returns. We are currently not subject to any income tax examinations. Due to our net operating losses, all tax years generally remain open in each jurisdiction.

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Results of Operations

For the Years Ended December 31, 2014 and 2013

	For the Year Ended December 31,	
(In millions)	2014	2013
Revenues	$69.5	$16.9
Cost of sales	9.4	1.7
Gross profit	60.1	15.2
Operating expenses:		
Research and development	43.5	29.2
Selling, general, and administrative	56.7	37.9
Total operating expenses	100.1	67.1
Loss from Operations	(40.1)	(51.9)
Interest expense	(14.0)	(6.8)
Adjustment to the fair value of common stock warrants	(1.1)	(10.7)
Other	2.6	0.1
Net Loss	$(52.5)	$(69.4)

Revenue

We recognized $17.3 million and $10.2 million in PROCYSBI net product sales for the fourth quarters of 2014 and 2013, respectively. Net product sales for the years ended December 31, 2014 and 2013 totaled $69.5 million and $16.9 million, respectively. The increase in revenue was driven by continued market penetration in both the United States and Europe. PROCYSBI became commercially available in the U.S. in June 2013 and in Europe in April 2014.

Cost of Sales

Prior to the approval of PROCYSBI by the FDA on April 30, 2013 and in Europe, prior to EMA approval on September 6, 2013, we recorded manufacturing costs relating to PROCYSBI as research and development expense. Subsequent to approval, we began capitalizing these costs as commercial inventory. As a result, our cost of sales for 2013 and 2014 will reflect a lower average per unit cost of goods than will be recorded in the future. Cost of sales primarily includes: raw materials and manufacturing costs for our commercial product PROCYSBI, amortization of licensing milestone payments, royalty fees due to UCSD on our net product sales, other indirect costs such as distribution, labeling, shipping and supplies, and provision for inventory expiration. Costs capitalized as inventory are expensed as cost of sales as product is sold.

During the year ended December 31, 2014, we recorded cost of sales of $9.4 million, primarily due to a $3.2 million provision for inventory expiration, royalties, and allocated manufacturing costs. During the year ended December 31, 2013, we recorded cost of sales of $1.7 million, including a $0.4 million reserve representing commercial inventory that was capitalized subsequent to FDA approval but written off due to an unanticipated minor change in the finished product presentation.

Research and Development

Research and development expenses include medical, clinical, regulatory, quality, pharmacovigilance and research salaries and benefits; expenses associated with the manufacturing and testing of PROCYSBI inventory for our

commercial launch in the United States and in Europe which were expensed prior to drug approvals; preclinical studies; clinical trials; regulatory and clinical consultants; research supplies and materials; amortization of intangible assets and allocated human resources and facilities expenses.

For the years ended December 31, 2014 and 2013, our research and development expenses were $43.5 million and $29.2 million, respectively. The increase in research and development expenses relates primarily to increased clinical product manufacture of RP103 for the potential treatment of HD, NASH, cystinosis extension, and other supporting study expenses and related employee compensation, partially offset by a reduction in Phase 3 cystinosis clinical trial expenses.

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The following table shows major program expenses recorded as research and development expenses.

Major Program Expenses Recorded as Research and Development

(In millions)	For the Year Ended December 31, 2014	2013
RP103:		
Cystinosis (pre-commercial and extension)	$12.9	$14.8
HD (clinical)	2.0	0.8
NASH (clinical)	1.9	2.0
Preclinical programs	2.0	1.1
Other programs	2.2	0.8
R&D personnel and other costs not allocated to programs	22.5	9.7
Total Research and Development Expenses	$43.5	$29.2

Selling, General and Administrative Expenses

Selling, general and administrative expenses primarily include commercial expenses related to marketing and sales efforts in the United States and EU, including marketing and pricing studies, advertising, sales force commissions and other expenses, and market access support activities; commercial launch expenses for PROCYSBI, including patient support activities such as reimbursement assistance and establishing a customer relationship management system for our PROCYSBI sales team; intellectual property, legal and audit fees, finance, executive and commercial operations salaries and benefits; and other administrative and facilities costs.

For the years ended December 31, 2014 and 2013, our selling, general and administrative expenses were $56.7 million and $37.9 million, respectively. The increase in selling, general and administrative expenses is primarily due to increased expenses related to commercial launch and ongoing operations and marketing activities for PROCYSBI, employee compensation, stock-compensation for employees and directors, accounting fees, legal fees and investor relations costs.

For the year ended December 31, 2013, our program expenses in selling, general and administrative expenses consisted primarily of pre-commercial and commercial launch expenses for PROCYSBI. The following table shows major program expenses recorded as selling, general and administrative expenses.

Major Program Expenses Recorded as Selling, General and Administrative Expenses

(In millions)	For the Year Ended December 31, 2014	2013
RP103:		
Cystinosis (pre-commercial and extension)	$6.7	$9.8
HD (clinical)	1.0	0.5
NASH (clinical)	0.1	0.1
Other programs	0.5	0.2
Total Selling, General, and Administrative Expenses	$8.3	$10.6

Interest Expense

Interest expense for the years ended December 31, 2014 and 2013 was $14.0 million and $6.8 million, respectively. The increase in interest expense was due primarily to an increase in royalty fees pursuant to the HC Royalty loan agreement based on net sales for the period. Also contributing to the increase was the issuance of $60 million of convertible notes in July 2014 and an amendment to the $50.0 million loan agreement that we entered into with HealthCare Royalty Partners II, L.P., or HC Royalty, in December 2012, which was amended in July 2014 to provide for an additional $10 million in term loan funding.

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Adjustment to the Fair Value of Common Stock Warrants

Adjustment to the fair value of common stock warrants were losses of $1.1 million and $10.7 million for the years ended December 31, 2014 and 2013, respectively. The decrease in fair value adjustment was due primarily to the decrease in the number of warrants outstanding.

Other Income

In 2014, we received a cash payment in the amount of $2.3 million from a stockholder in disgorgement of alleged short-swing profits under Section 16(b) of the Securities Exchange Act of 1934. This amount is recorded as Other Income on our consolidated financial statements.

Current Status of Major Programs

Please refer to the Item 1 of this Annual Report on Form 10-K for a detailed discussion of each of our major programs. We currently have product candidates in clinical development as potential treatments for HD, pediatric NASH, Leigh syndrome and other mitochondrial disorders and ALDH2. Our preclinical programs are based upon bioengineered novel drug candidates that are designed to target cancer and other diseases. We continue efforts to out-license Convivia in additional territories.

Any of our major programs could be partnered for further development and/or could be accelerated, slowed or ceased due to scientific results or challenges in obtaining funding. We anticipate that we will need additional funding in order to pursue our plans beyond the next 24 months. In addition, the timing and costs of development of our programs beyond the next 24 months is highly uncertain and difficult to estimate. See Part I, Item 1A of this Annual Report on Form 10-K titled "Risk Factors" for further discussion about the risks and uncertainties pertaining to drug development.

For the Four Months Ended December 31, 2012 and the Fiscal Year Ended August 31, 2012

(In millions)	For the Four Months Ended December 31, 2012	For the Year Ended August 31, 2012
Revenues	$ -	$ -
Operating expenses:		
Research and development	8.9	21.4
Selling, general, and administrative	9.0	14.7
Total operating expenses	17.9	36.2
Loss from Operations	(17.9)	(36.2)
Interest expense	(0.1)	(0.0)
Adjustment to the fair value of common stock warrants	(1.5)	(3.2)
Other	0.2	0.7
Net Loss	$ (19.3)	$ (38.6)

Research and Development

For the four months ended December 31, 2012, our research and development expenses consisted primarily of costs associated with the manufacturing and testing of clinical and commercial materials in anticipation for our approval and commercial launch of RP103 for cystinosis, clinical trial research expenses and employee compensation.

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For the year ended August 31, 2012, research and development expenses include medical, clinical, regulatory and scientists' compensation and benefits, lab collaborations, preclinical studies, clinical trials, amortization of intangible assets and allocated human resources and facilities expenses.

Major Program Expenses Recorded as Research and Development

(In millions)	For the Four Months Ended December 31, 2012	For the Year Ended August 31, 2012
RP103: All indications (clinical/pre-commercial)	$ 5.1	$ 18.2
Preclinical programs	0.2	0.0
Other programs	0.2	1.7
R&D personnel and other costs not allocated to programs	3.4	1.5
Total Research and Development Expenses	$ 8.9	$ 21.4

General and Administrative Expenses

For the four months ended December 31, 2012, our general and administrative expenses consisted primarily of expenses for pre-commercial operations requirements for RP103 for the potential treatment of cystinosis, employee compensation, stock compensation for employees and directors, legal fees and investor relations costs. Additional major program expenses include patent fees and patent expenses which were recorded as general and administrative expenses as these fees are to support patent applications (not issued patents) and expenses related to the pre-commercial launch of RP103 for the potential treatment of cystinosis.

For the year ended August 31, 2012, general and administrative expenses included finance, executive and sales and marketing compensation and benefits, pre-commercial expenses, such as reimbursement and marketing studies, corporate costs, such as legal and auditing fees, business development expenses, travel, board of director fees and expenses, investor relations expenses, intellectual property costs associated with filed (but not issued) patents, administrative consulting and allocated human resources and facilities costs.

Major Program Expenses Recorded as General and Administrative Expenses

For the four months ended December 31, 2012 and the fiscal year ended August 31, 2012, our program expenses in general and administrative expenses consisted primarily of pre-commercial launch expenses for RP103, such as market research and market access studies.

(In millions)	For the Four Months Ended December 31, 2012	For the Year Ended August 31, 2012
RP103: All indications (clinical/pre-commercial)	$ 3.2	$ 2.7
Other programs	0.2	0.1
Total Selling, General, and Administrative Expenses	$ 3.4	$ 2.8

Adjustment to the Fair Value of Common Stock Warrants

Adjustment to the fair value of common stock warrants was a loss of approximately $1.5 million for the four months ended December 31, 2012. Adjustment to the fair value of common stock warrants was a loss of approximately $3.2 million for the year ended August 31, 2012.

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Liquidity and Capital Resources

Capital Resources

As of December 31, 2014, we had $149.6 million in cash and cash equivalents, of which $5.4 million is held by our foreign subsidiaries, $29.1 million in current liabilities and $142.5 million of net working capital. During the year ended December 31, 2014, we raised $66 million of net proceeds from modification of our loan agreement with HC Royalty Partners and the issuance of convertible notes, $44.8 million in proceeds after commissions under our at-the-market ("ATM") common stock sales agreement, $1.8 million net proceeds from warrant exercises and $6.8 million net proceeds from stock option exercises and our employee stock purchase plan. We believe that our cash balance will be sufficient to meet our projected operational requirements and obligations at least through 2016.

Under the terms of the HC Royalty loan agreement executed on December 20, 2012, we received $23.4 million in net proceeds from the first tranche of the loan at closing in December 2012. We received an additional $23.7 million in net proceeds in May 2013 from the second tranche upon FDA approval of RP103 for the management of cystinosis. In July 2014, we modified our original December 2012 loan agreement to provide for an additional $10 million in term loan funding. The loan matures on March 31, 2020, bears interest at an annual fixed rate of 8.0% (after the July 2014 modification) and has a synthetic royalty, tiered down, based on a percentage of net product sales. The loan is interest-only until June 2015. In July 2014, we also sold $60 million of convertible senior notes, which bear a fixed interest rate of 8.0% until maturity in August 2019, if not yet converted. The proceeds from the loans are being used primarily to fund the commercialization of PROCYSBI for the management of cystinosis, advance our development programs and for general corporate purposes.

On April 30, 2012, we entered into a Sales Agreement with Cowen and Company, or Cowen, to sell shares of our common stock, with aggregate gross sales proceeds of up to $40 million, from time to time through an "at the market" equity offering program under which Cowen acted as sales agent. We paid a 3% commission to Cowen on all sales pursuant to this Sales Agreement.

On July 3, 2013, we amended and restated the Sales Agreement to increase the aggregate gross sales proceeds that may be raised to $100 million. Cumulatively through December 31, 2014, we sold 12,569,914 shares under the ATM offerings at a weighted-average selling price of $7.96 per share for net proceeds of approximately $97 million. During the three months ended December 31, 2014, we sold 4,970,440 shares under the ATM for net proceeds of approximately $45 million.

As of February 20, 2015, there were warrants exercisable for an aggregate of 334,764 shares of our common stock outstanding.

Future Funding Requirements

We will need to raise additional capital through the sale of either equity or debt or both to fund our operations and to, among other activities, continue to commercialize PROCYSBI and develop RP103 for the potential treatment of other indications. Our future capital requirements may be substantial, and will depend on many factors, including:

- The continuing sales of PROCYSBI in the United States and Europe;
- The ongoing costs of establishing and maintaining sales and marketing capabilities in the United States, Europe and other countries;
- Our ability to negotiate reimbursement and pricing of PROCYSBI in various countries outside of the United States;
- The cost of our manufacturing-related activities in support of PROCYSBI and RP103;
- The cost of activities and outcomes related to the regulatory submission of cysteamine bitartrate delayed-release capsules in Canada;

- The cost of additional clinical trials in order to obtain regulatory approvals for PROCYSBI in non-U.S. and non-European countries;
- The timing and cost of our ongoing clinical programs for RP103, including: evaluating PROCYSBI in treatment-naïve cystinosis patients, and other supportive studies; evaluating RP103 as a potential treatment for HD; evaluating RP103 as a potential treatment for NASH in children; evaluating RP103 as a potential treatment for Leigh syndrome and other mitochondrial disorders;

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- The cost of regulatory submissions, as well as the preparation, initiation and execution of clinical trials in potential new clinical indication using RP103;
- The cost of evaluating and potentially acquiring or in-licensing new drug compound(s) for potential clinical development and commercialization; and
- The cost of filing, surveillance around, prosecuting, defending and enforcing patent claims.

There can be no assurance that we will be successful in raising sufficient funds when needed. Additional financing may not be available in amounts or on terms satisfactory to us or at all.

Research and Development Activities

We plan to conduct further research and development, to support several clinical trials for RP103, improve upon our internal discovery molecules and in-licensed technology and continue business development efforts for our preclinical and other clinical-stage product candidates in the next 12 months. We plan to conduct research and development activities by our own laboratory staff and also by engaging contract research organizations, clinical research organizations and contract manufacturing organizations. We also plan to incur costs for the production of our clinical study drug candidate RP103 for the potential treatment of HD and NASH; for production of RP103 for additional clinical trials in cystinosis; clinical and medical advisors; and consulting and collaboration fees. We anticipate that our research and development costs will increase during the next 12 months primarily due to the addition of new studies in support of cystinosis, HD, pediatric NASH, Leigh syndrome and other indications.

Selling, General and Administrative Activities

Selling, general and administrative costs in the next 12 months will consist primarily of sales activities surrounding the sale of PROCYSBI in the United States and Europe and the commercial launch of PROCYSBI in additional countries in Europe, of legal, business development, tax and accounting fees, patent legal fees, investor relations expenses, board fees and expenses, insurance, rent and facility support expenses. We anticipate that selling, general and administrative expenses will continue to increase in support of PROCYSBI sales growth, as well as an increase in facilities and administrative expenses to support our anticipated growth.

Capital Expenditures

In the next 12 months, we expect to increase our capital expenditures on laboratory and office equipment and computer software and hardware as we continue to increase our staff in 2015.

Contractual Obligations

Contractual Obligations with UCSD Relating to the Acquisition of the DR Cysteamine (RP103) License

Pursuant to our license agreement with UCSD, we are obligated to pay milestone payments (ranging in size for orphan and non-orphan indications) upon the occurrence of certain events during the life of the license agreement. These include a royalty on commercial net sales from products developed pursuant to the agreement, a percentage of sublicense fees, a percentage of sublicense royalties, and a minimum annual royalty. Under the license agreement, we are obligated to fulfill predetermined milestones within a specified number of years from the effective date of the agreement, depending on the indication. Cumulatively, we have expensed approximately $0.9 million in milestone payments to UCSD based upon the initiation of clinical trials in cystinosis, Huntington's disease and NASH and on regulatory filings in cystinosis. In March 2012, we filed an MAA with the EMA, as well as an NDA with the FDA for RP103 for the potential treatment of cystinosis. In conjunction with the achievement of MAA/NDA filing milestone, we paid additional milestone payments to UCSD pursuant to this license. Based on approval of RP103 by the FDA on April 30, 2013 we paid a milestone license of $0.75 million which was capitalized as commercial IP and is being

amortized as expense in cost of sales over the life of the patent. Based on approval by the EMA of RP103 on September 6, 2013, we paid a milestone license of $0.5 million which was capitalized as commercial IP and is being amortized as expense in cost of sales over the life of the patent. In 2013, we began paying UCSD royalties based upon our net sales of PROCYSBI. Other future milestones will be payable based on other regulatory approvals and clinical trial milestones.

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Other Contractual Obligations

We have contractual obligations under our capital and operating leases and other obligations related to research and development activities, purchase commitments and licenses. Information about these obligations as of December 31, 2014 is presented in the table below:

(In thousands)	< 1 year	1 - 3 Years	3 - 5 Years	> 5 Years	Total
Debt principal	$9,000	$24,000	$24,000	$3,000	$60,000
Convertible notes	-	-	60,000	-	60,000
Operating lease obligations	1,553	3,768	3,800	3,329	12,450
Purchase commitments and research and development/clinical	6,979	831	108	300	8,218
Total	$17,532	$28,599	$87,908	$6,629	$140,668

We maintain several contracts with contract manufacturers, clinical organizations and clinical sites, drug labelers and distributors and research organizations, primarily to assist with clinical research and clinical manufacturing for our cystinosis and HD programs and our NASH clinical collaboration. The future commitments pursuant to these agreements, some of which include estimates of amounts or timing of payments, are included in the table above as research and development and purchase commitments.

We are also subject to contingent payments related to various development activities totaling approximately $17.1 million, which are primarily due upon the achievement of certain development and commercial milestones if such milestones occur before certain dates in the future. These contingent payments are not included in the table above as we cannot reliably predict their timing or occurrence.

In conjunction with our HC Royalty loan agreement, we have contractual interest payments that began in December 2012 at a fixed rate of 10.75% plus a percentage of product revenue. In July 2014, these fixed interest payments were amended to 8.00%. We also issued senior convertible notes which bear fixed interest of 8.00%. The fixed interest amount that remains committed through the term of the amended loan agreement and convertible senior notes is approximately $36.2 million.

Off-Balance Sheet Arrangements

We do not have any outstanding derivative financial instruments, off-balance sheet guarantees, interest rate swap transactions or foreign currency contracts. We do not engage in trading activities involving non-exchange traded contracts.

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ITEM 7A: QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Market risk represents the risk of changes in the value of market risk sensitive instruments caused by fluctuations in interest rates, foreign exchange rates and commodity prices. We are exposed to various market risks that may arise from adverse changes in market rates and prices, such as foreign exchange rate and interest rate fluctuations. We do not enter into derivatives or other financial instruments for trading or speculative purposes.

Foreign Exchange Risk

A majority of our assets and liabilities are maintained in the United States in U.S. dollars and a majority of our expenditures are transacted in U.S. dollars. We are subject to foreign exchange risk for the operations of Raptor Pharmaceuticals Europe B.V., Raptor Pharmaceuticals France SAS, and Raptor Pharmaceuticals Germany GmbH, which use the Euro as their functional currency. We do not believe that a hypothetical one percentage point fluctuation in the U.S. dollar exchange rate would materially affect our consolidated financial position, results from operations or cash flows as of December 31, 2014. We do not currently hedge our foreign currency transactions.

Interest Rate Risk

As of December 31, 2014, we had approximately $137.9 million in cash equivalent money market accounts, yielding approximately 0.06% per year. A hypothetical one percentage point decline in interest rates would not have materially affected our consolidated financial position, results of operations or cash flows as of December 31, 2014.

ITEM 8: FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

The information required to be filed in this item appears on pages 91 to 120 of this Annual Report on Form 10-K.

Documents filed as part of this Annual Report on Form 10-K:

Financial Statements

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PART II – FINANCIAL INFORMATION

ITEM 9: CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

ITEM 9A: CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

Disclosure controls and procedures are controls and other procedures that are designed to ensure that information required to be disclosed in our reports filed or submitted under the Securities Exchange Act of 1934, as amended, is recorded, processed, summarized and reported, within the time periods specified in the Securities and Exchange Commission's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed in our reports filed under the Exchange Act is accumulated and communicated to management, including our principal executive officer and our principal financial officer, as appropriate, to allow timely decisions regarding required disclosure. As of the end of the period covered by this report, the Company carried out an evaluation under the supervision and with the participation of its management, including the Company's Chief Executive Officer ("CEO") and its Chief Financial Officer ("CFO"), of the effectiveness of the design and operation of the Company's disclosure controls and procedures in ensuring that material information required to be disclosed in the Company's reports filed or submitted under the Exchange Act, has been made known to them in a timely fashion. Based on this evaluation, the CEO and CFO concluded that the Company's disclosure controls and procedures were not effective as of December 31, 2014 due to a material weakness in our internal control over financial reporting related to our inventory costing and overhead allocations for our commercial product PROCYSBI, which is disclosed below. Notwithstanding the identified material weakness, management of the Company does not believe that these deficiencies had an adverse effect on our reported operating results or financial condition and management has determined that the financial statements and other information included in this Annual Report on Form 10-K and other periodic filings present fairly in all material respects the financial position and results of operations at and for the periods presented in accordance with the accounting principles generally accepted in the United States of America ("GAAP").

Management's Annual Report on Internal Control over Financial Reporting

Management of the Company is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act. The Company's internal control over financial reporting is designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. The Company's internal control over financial reporting includes those policies and procedures that (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the Company; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the Company are being made only in accordance with authorizations of management and directors of the Company; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the Company's assets that could have a material effect on the consolidated financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. All control systems have inherent limitations so that no evaluation of controls can provide absolute assurance that all control issues are detected. A control system, no matter how well conceived and operated, can provide only

reasonable, not absolute, assurance that the objectives of the internal control system are met. We are continuously seeking to improve the efficiency and effectiveness of our operations and of our internal controls. This results in refinements to processes throughout our organization. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Under the supervision and with the participation of our management, we assessed the effectiveness of the Company's internal control over financial reporting as of December 31, 2014, based on the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission ("COSO") in the 2013 Internal Control-Integrated Framework. Based on the results of our assessment, we concluded that there was a material weakness in the design and operating effectiveness of our internal control over financial reporting related to our inventory costing and overhead allocations for our commercial product PROCYSBI as of December 31, 2014. A material weakness is defined as a deficiency or a combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected on a timely basis.

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During the year ended December 31, 2014, we determined that certain management review controls, including those designed to provide oversight over our inventory costing and tracking systems were not effective. Our findings related to both the design and operating effectiveness of these controls. Although certain adjustments identified during the year related to a variety of accounts and were not material, we concluded that these control deficiencies could lead to misstatements in the aforementioned accounts and related disclosures, which would give rise to a reasonable possibility that a material misstatement of the consolidated financial statements would not be prevented or detected. Accordingly, management has determined that these control deficiencies collectively constitute a material weakness. Given this material weakness, management concluded that the Company did not maintain effective internal control over financial reporting as of December 31, 2014, based on the criteria in the 2013 Internal-Control Integrated Framework issued by the COSO.

Grant Thornton LLP, an independent registered public accounting firm, has audited the effectiveness of the Company's internal control over financial reporting as of December 31, 2014 as stated in their report, which is referenced in the index appearing under Item 8.

Material Weakness and Remediation Activities

As part of our assessment of internal control over financial reporting as of December 31, 2014, during the fourth quarter of 2014, we determined that our reviews of our inventory costing and overhead allocations for our commercial product PROCYSBI were not performed at a sufficiently detailed level to detect errors in our inventory and related accounts.

With the oversight of management and our Audit Committee, we have initiated actions to address the root causes of the material weakness identified in 2014. These following actions are planned to be implemented in 2015.

- We will implement additional automated controls related to our standard costing overhead model, add additional requirements to our tolerances, and add additional and more precise general and management review controls to ensure that all available information is properly considered and reconciled.

- We will add additional personnel as needed to support our inventory supply chain process, including personnel in senior level oversight roles to improve the precision and effectiveness of the review function throughout the company.

The material weakness will not be considered remediated until the remedial controls operate for a sufficient period.

ITEM 9B: OTHER INFORMATION

None.

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PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information required by Item 10 is incorporated herein by reference to the definitive Proxy Statement to be filed with the SEC pursuant to Regulation 14A within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

ITEM 11. EXECUTIVE COMPENSATION

The information required by Item 11 is incorporated herein by reference to the definitive Proxy Statement to be filed with the SEC pursuant to Regulation 14A within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The information required by Item 12 is incorporated herein by reference to the definitive Proxy Statement to be filed with the SEC pursuant to Regulation 14A within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information required by Item 13 is incorporated herein by reference to the definitive Proxy Statement to be filed with the SEC pursuant to Regulation 14A within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

The information required by Item 14 is incorporated herein by reference to the definitive Proxy Statement to be filed with the SEC pursuant to Regulation 14A within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

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PART IV

ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES

The information required to be filed in this item appears on pages 91 to 120 of this Annual Report on Form 10-K.

(a) Documents filed as part of this Annual Report on Form 10-K:

(1) Index list to Consolidated Financial Statements:

(2) Schedule II is included on page 121 of this report. All other schedules are omitted because they are not required or the required information is included in the financial statements or notes thereto.

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Exhibits

The following exhibits are filed as part of, or incorporated by reference into this Annual Report on Form 10-K:

Exhibit Number	Exhibit Description	Incorporated by Reference			Filed Here with
		Form	Date	Exhibit Number	
2.1	Agreement and Plan of Merger and Reorganization, dated June 7, 2006, among Axonyx Inc., Autobahn Acquisition, Inc. and TorreyPines Therapeutics, Inc.	S-4	7/25/2006	Annex A	
2.2	Amendment No. 1 to Agreement and Plan of Merger and Reorganization, dated August 25, 2006, among Axonyx Inc., Autobahn Acquisition, Inc. and TorreyPines Therapeutics, Inc.	S-4/A	8/25/2006	Annex A	
2.3	Agreement and Plan of Merger and Reorganization, dated July 27, 2009, among ECP Acquisition, Inc., Raptor Pharmaceuticals Corp. and TorreyPines Therapeutics, Inc.	8-K	7/28/2009	2.1	
3.1	Certificate of Incorporation of the Registrant	8-K	10/10/2006	3.1	
3.2	Amended and Restated Bylaws of the Registrant	8-K	2/26/2014	3.1	
3.3	Certificate of Amendment to the Articles of Incorporation of Axonyx Inc., filed with the Secretary of State of the State of Nevada, effecting an 8-for-1 reverse split of the Registrant's common stock and changing the name of the Registrant from Axonyx Inc. to TorreyPines Therapeutics, Inc.	8-K	10/10/2006	3.3	
3.4	Articles of Conversion of TorreyPines Therapeutics, Inc., filed with the Secretary of State of the State of Nevada, changing the state of incorporation of the Registrant	8-K	10/10/2006	3.4	
3.5	Certificate of Conversion of TorreyPines Therapeutics, Inc., filed with the Secretary of State of the State of Delaware	8-K	10/10/2006	3.5	
3.6	Certificate of Amendment to Certificate of Incorporation of TorreyPines Therapeutics, Inc.	8-K	10/5/2009	3.1	
3.7	Certificate of Merger of ECP Acquisition, Inc. with and into Raptor Pharmaceuticals Corp.	8-K	10/5/2009	3.2	
4.1	Specimen common stock certificate of the Registrant	8-K	10/5/2009	4.7	
4.2(a)	Rights Agreement, dated as of May 13, 2005, between Registrant and The Nevada Agency and Trust Company, as Rights Agent	8-K	5/16/2005	99.2	
4.2(b)	Amendment to Rights Agreement, dated as of June 7, 2006, between Registrant and The Nevada Agency and Trust Company, as Rights Agent	8-K	6/12/2006	4.1	
4.2(c)	Amendment to Rights Agreement, dated as of October 3, 2006, between Registrant and The Nevada Agency and Trust Company, as Rights Agent	10-K	3/29/2007	4.19	
4.2(d)	Amendment to Rights Agreement, dated as of July 27, 2009, to the Rights Agreement dated May 13, 2005 between Registrant and American Stock Transfer and Trust Company (replacing The Nevada Agency and Trust Company)	8-K	7/28/2009	4.1	
4.2(e)	Amendment to Rights Agreement, dated August 6, 2010, by and between Registrant and American Stock Transfer & Trust Company, LLC	8-K	8/10/2010	4.2	
4.3	Form of Warrant, dated September 27, 2005, issued to Oxford Financial and Silicon Valley Bank	10-K	3/29/2007	4.16	
4.4*	Warrant, dated December 14, 2007, issued to Flower Ventures, LLC	10QSB**	4/15/2008	4.1	

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4.5*	Warrant Agreement Amendment, dated December 17, 2009, between Flower Ventures, LLC and the Registrant	10-Q	4/9/2010	4.15
10.1#	TorreyPines Therapeutics, Inc. 2006 Equity Incentive Plan	8-K	10/4/2006	10.1
10.2#	Form of Stock Option Agreement under TorreyPines Therapeutics, Inc. 2006 Equity Incentive Plan	8-K	10/4/2006	10.2
10.3#	2006 Equity Incentive Plan of Raptor Pharmaceuticals Corp., as amended	S-8**	2/28/2007	4.3
10.4#	Amendment to 2006 Equity Incentive Plan of Raptor Pharmaceuticals Corp.	10-K/A**	12/23/2008	10.5
10.5#	Raptor Pharmaceutical Corp. 2010 Stock Incentive Plan	DEF14A	2/5/2010	Appendix A
10.6#	Amendments to the Raptor Pharmaceutical Corp. 2010 Stock Incentive Plan	S-8	4/26/2011	4.15
10.7#	Form of Award Agreement under the Raptor Pharmaceutical Corp. 2010 Stock Incentive Plan	8-K	9/28/2011	10.1
10.8#	Amendment to the Raptor Pharmaceutical Corp. 2010 Stock Incentive Plan	8-K	7/25/2013	10.1
10.9	Securities Purchase Agreement, dated December 17, 2009, between the investors signatories thereto and the Registrant	8-K	12/18/2009	10.1
10.10	Securities Purchase Agreement, dated August 9, 2010, among the investors signatory thereto and the Registrant	8-K	8/10/2010	10.1
10.11	Securities Purchase Agreement, dated August 9, 2010, among the investors signatory thereto and the Registrant	8-K	8/10/2010	10.2
10.12	Registration Rights Agreement, dated April 16, 2010, between Lincoln Park Capital Fund, LLC and the Registrant	8-K	4/22/2010	10.2
10.13	Registration Rights Agreement, dated August 12, 2010, among the signatories thereto and the Registrant	8-K	8/13/2010	10.3
10.14#	Employment Agreement, dated May 15, 2006, between Dr. Todd Zankel and Raptor Pharmaceuticals Corp.	8-K**	5/26/2006	10.6
10.15#	First Amendment to Employment Agreement, dated January 1, 2009, between Dr. Todd Zankel and Raptor Pharmaceuticals Corp.	8-K**	1/5/2009	10.3
10.16#	Employment Agreement, dated September 7, 2007, between Thomas E. Daley and Raptor Therapeutics Inc.	10-QSB**	1/14/2008	10.1
10.17#	First Amendment to Employment Agreement, dated January 1, 2009, between Thomas E. Daley and Raptor Pharmaceuticals Corp.	8-K**	1/5/2009	10.4
10.18#	Offer Letter, dated April 8, 2009, between and Dr. Patrice Rioux and Raptor Therapeutics Inc.	8-K**	4/14/2009	10.1
10.19++#	Offer Letter, dated January 1, 2011, between Patrick Reichenberger and Raptor Therapeutics Inc.	10-K	11/14/2011	10.17
10.20++#	Employment Agreement, dated April 15, 2012, between Henk Doude van Troostwijk and Raptor Pharmaceuticals Europe B.V.	10-Q	7/10/2012	10.1
10.21++#	Employment Agreement, dated September 10, 2012, between Kim R. Tsuchimoto and the Registrant	8-K	9/12/2012	10.3
10.22#	Employment Agreement, dated September 25, 2012, between Kathy Powell and the Registrant	8-K	10/1/2012	10.1
10.23++	Research and License Agreement, dated May 10, 2004, between TPTX, Inc. and Life Science Research Israel Ltd.	8-K	10/10/2006	10.2

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10.24	Asset Purchase Agreement, dated October 17, 2007, between Convivia, Inc., Raptor Therapeutics, Inc. and Raptor Pharmaceuticals Corp.	10QSB**	1/14/2008	10.3
10.25	Merger Agreement, dated December 14, 2007, between Encode Pharmaceuticals, Inc., Raptor Therapeutics, Inc. and Raptor Pharmaceuticals Corp.	10QSB/A**	4/15/2008	10.1
10.26++	Pharmaceutical Development Services Agreement, dated January 7, 2008, between Raptor Therapeutics Inc. and Patheon Pharmaceuticals Inc.	10QSB/A**	4/15/2008	10.2
10.27	Form Indemnity Agreement	8-K	12/15/2009	10.1
10.28++	Manufacturing Services Agreement, dated November 15, 2010, between Patheon Pharmaceuticals Inc. and Raptor Therapeutics, Inc.	POS AM	11/23/2010	10.53
10.29++	API Supply Agreement, dated November 15, 2010, between Cambrex Profarmaco Milano and Raptor Therapeutics Inc.	POS AM	11/23/2010	10.54
10.30++	Cooperative Research and Development Agreement for Extramural-PHS Clinical Research, dated December 15, 2011, between the U.S. Department of Health and Human Services, as represented by the National Institute of Diabetes and Digestive and Kidney Diseases, an institute or center of the National Institutes of Health, and Raptor Therapeutics Inc.	10-Q	4/9/2012	10.1
10.31++	Second Amendment to License Agreement, effective October 30, 2012, between The Regents of the University of California and Raptor Therapeutics, Inc.	10-KT	3/14/2013	10.37
10.32++	Wholesale Product Purchase Agreement, dated April 3, 2013, between Accredo Health Group, Inc. and Raptor Pharmaceuticals Inc.	10-Q	8/9/2013	10.1
10.33++	Pharmacy Services Agreement, dated April 3, 2013, between Accredo Health Group, Inc. and Raptor Pharmaceuticals Inc.	10-Q	8/9/2013	10.2
10.34	Office Lease, dated April 18, 2013, between Hamilton Marin, LLC and Raptor Pharmaceuticals Corp.	10-Q	8/9/2013	10.3
10.35	First Amendment to Lease, dated June 10, 2013, between Hamilton Marin, LLC and Raptor Pharmaceuticals Corp.	10-Q	8/9/2013	10.4
10.36++	Amendment to Manufacturing Services Agreement, dated April 5, 2012, between Patheon Pharmaceuticals Inc. and Raptor Therapeutics, Inc.	10-Q	8/9/2013	10.5
10.37++	Second Amendment to Manufacturing Services Agreement, dated June 21, 2013, between Patheon Pharmaceuticals Inc. and Raptor Therapeutics, Inc.	10-Q	8/9/2013	10.6
10.38	Convertible Note Purchase Agreement, dated as of July 1, 2014, among Registrant, as Issuer, HealthCare Royalty Partners II, L.P., HCRP Overflow Fund, L.P. and MOLAG Healthcare Royalty, LLC, each as Holder, and the Guarantors party thereto	8-K	7/2/2014	10.1
10.39#	Amended and Restated Employment Agreement, dated as of July 7, 2014, by and between Julie Anne Smith and Registrant	8-K	7/8/2014	10.1
10.40#	Transition and Separation Agreement, dated as of July 7, 2014, by and between Christopher Starr, Ph.D. and Registrant	8-K	7/8/2014	10.1
10.41	Second Amended and Restated Sales Agreement, dated as of August 21, 2014, between Registrant and Cowen and Company, LLC	8-K	8/21/2014	10.1
10.42++	Amended and Restated Loan Agreement, dated as of July 1, 2014, by and among Healthcare Royalty Partners II, L.P., Registrant and the Guarantors party thereto	8-K	8/21/2014	10.1
10.43#	Separation Agreement, dated as of October 21, 2014, by and between Georgia Erbez and Registrant	8-K	10/24/2014	10.1
10.44#	Executive Employment Agreement, dated as of January 2, 2015, by and between Michael Smith and Registrant	8-K	1/7/2015	10.1

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10.45#	Raptor Pharmaceutical Corp. 2015 Employment Commencement Stock Incentive Plan	X
10.46#	Form of Stock Option Agreement under Raptor Pharmaceutical Corp. 2015 Employment Commencement Stock Incentive Plan	X
10.47#	Executive Employment Agreement, dated as of October 21, 2014, by and between David Happel and Registrant	X
10.48#	Executive Employment Agreement, dated as of January 2, 2015, by and between Krishna Polu, M.D. and Registrant	X
10.49	Third Amendment to License Agreement, dated as of March 1, 2013, between The Regents of the University of California and Raptor Pharmaceuticals, Inc.	X
10.50	Fourth Amendment to License Agreement, dated as of December 16, 2013, between The Regents of the University of California and Raptor Pharmaceuticals, Inc.	X
21.1	Subsidiaries of the Registrant	X
23.1	Consent of Grant Thornton LLP, Independent Registered Public Accounting Firm to the Registrant	X
23.2	Consent of Burr Pilger Mayer, Inc., Former Independent Registered Public Accounting Firm to the Registrant	X
24.1	Power of Attorney (included in the signature page hereto)	X
31.1	Certification of Julie Anne Smith, Chief Executive Officer and Director	X
31.2	Certification of Michael P. Smith, Chief Financial Officer, Secretary and Treasurer	X
32.1	Certification of Julie Anne Smith, Chief Executive Officer and Director, and of Michael P. Smith, Chief Financial Officer, Secretary and Treasurer	X
101.INS	XBRL Instance Document	X
101.SCH	XBRL Taxonomy Extension Schema Document	X
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document	X
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document	X
101.LAB	XBRL Taxonomy Extension Labels Linkbase Document	X
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document	X

* The Raptor Pharmaceuticals Corp. warrants set forth in Exhibits 4.4 and 4.5 have been converted into warrants of the Registrant and the exercise price of such warrants and number of shares of common stock issuable thereunder have been converted as described in Item 1.01 (under the section titled, "Background") of the Registrant's Current Report on Form 8-K, filed on October 5, 2009.

** Incorporated by reference from the indicated filing of Raptor Pharmaceuticals Corp. rather than that of the Registrant.

# Indicates a management contract or compensatory plan or arrangement.

++ Certain information omitted pursuant to a request for confidential treatment filed separately with and granted by the SEC.

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SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

RAPTOR PHARMACEUTICAL CORP.

Dated: March 2, 2015 By: /s/ Michael Smith
Michael Smith
Chief Financial Officer, Secretary and Treasurer
(Principal Financial Officer)

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Julie A. Smith and Michael Smith, his or her attorney-in-fact, with the power of substitution, for him or her in any and all capacities, to sign any amendments to this Annual Report on Form 10-K and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, hereby ratifying and confirming all that each of said attorneys-in-fact, or his or her substitute or substitutes, may do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated:

Signatures	Title	Date
/s/ Julie A. Smith Julie A. Smith	Chief Executive Officer and Director (Principal Executive Officer)	March 2, 2015
/s/ Michael Smith Michael Smith	Chief Financial Officer, Secretary and Treasurer (Principal Financial Officer and Principal Accounting Officer)	March 2, 2015
/s/ Raymond W. Anderson Raymond W. Anderson	Director	March 2, 2015
/s/ Suzanne L. Bruhn Suzanne L. Bruhn, Ph.D.	Director	March 2, 2015
/s/ Richard L. Franklin Richard L Franklin, M.D., Ph.D.	Director	March 2, 2015
/s/ Georges Gemayel Georges Gemayel, Ph.D.	Director	March 2, 2015
/s/ Llew Keltner Llew Keltner, M.D., Ph.D.	Director	March 2, 2015
/s/ Gregg Lapointe Gregg Lapointe	Director	March 2, 2015

/s/ Erich Sager Erich Sager	Director	March 2, 2015
/s/ Christopher M. Starr Christopher M. Starr, Ph.D.	Director	March 2, 2015

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RAPTOR PHARMACEUTICAL CORP.

CONSOLIDATED FINANCIAL STATEMENTS,

REPORTS OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

For Inclusion in Annual Report on Form 10-K Filed With

Securities and Exchange Commission

December 31, 2014

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RAPTOR PHARMACEUTICAL CORP.

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders
of Raptor Pharmaceutical Corp.

We have audited the accompanying consolidated balance sheets of Raptor Pharmaceutical Corp. (a Delaware corporation) and subsidiaries (the "Company") as of December 31, 2014 and 2013, and the related consolidated statements of operations and comprehensive loss, stockholders' equity (deficit), and cash flows for the years then ended and for the four month period ended December 31, 2012. Our audits of the basic consolidated financial statements included the financial statement schedule listed in the index appearing under Item 15(a)(2). These financial statements and financial statement schedule are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements and financial statement schedule 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. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of Raptor Pharmaceutical Corp. and subsidiaries as of December 31, 2014 and 2013, and the results of their operations and their cash flows for the years then ended and for the four month period ended December 31, 2012 in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the related financial statement schedule, when considered in relation to the basic consolidated financial statements taken as a whole, presents fairly, in all material respects, the information set forth therein.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the Company's internal control over financial reporting as of December 31, 2014, based on criteria established in the 2013 Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO), and our report dated March 2, 2015 expressed an adverse opinion thereon.

/s/ GRANT THORNTON LLP
San Francisco, California
March 2, 2015

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders of
Raptor Pharmaceutical Corp.

We have audited the internal control over financial reporting of Raptor Pharmaceutical Corp. (a Delaware corporation) and subsidiaries (the "Company") as of December 31, 2014, based on criteria established in the 2013 Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Management's Annual Report on Internal Control over Financial Reporting (“Management’s Report”). Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit.

We conducted our audit 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 effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

A material weakness is a deficiency, or combination of control deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of the Company’s annual or interim financial statements will not be prevented or detected on a timely basis. The following material weakness has been identified and included in management’s assessment: management has determined that its reviews of inventory costing and overhead allocations for its commercial product, PROCYSBI, were not performed at a sufficiently detailed level to detect errors in inventory and related accounts.

In our opinion, because of the effect of the material weakness described above on the achievement of the objectives of the control criteria, the Company has not maintained effective internal control over financial reporting as of December 31, 2014, based on criteria established in the 2013 Internal Control—Integrated Framework issued by COSO.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated financial statements of the Company as of and for the year ended December 31, 2014. The

material weakness identified above was considered in determining the nature, timing, and extent of audit tests applied in our audit of the 2014 consolidated financial statements, and this report does not affect our report dated March 2, 2015 which expressed an unqualified opinion on those financial statements.

We do not express an opinion or any other form of assurance on management's statements referring to corrective actions to be taken after December 31, 2014 relative to the aforementioned material weakness in internal control over financial reporting.

/s/ GRANT THORNTON LLP
San Francisco, California
March 2, 2015

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders of Raptor Pharmaceutical Corp.

We have audited the accompanying consolidated statements of comprehensive loss, shareholders' equity (deficit), and cash flows of Raptor Pharmaceutical Corp. and its subsidiaries (the "Company") (a development stage enterprise) for each of the two years in the period ended August 31, 2012. These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated 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. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the results of operations and cash flows of Raptor Pharmaceutical Corp. and its subsidiaries for each of the two years in the period ended August 31, 2012, in conformity with accounting principles generally accepted in the United States of America.

Burr Pilger Mayer, Inc.
San Francisco, California
November 13, 2012

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RAPTOR PHARMACEUTICAL CORP.
CONSOLIDATED BALANCE SHEETS
(In Thousands, except shares and per share data)

	December 31,	
	2014	2013
ASSETS		
Current assets:		
Cash and cash equivalents	$149,613	$83,052
Restricted cash	1,562	500
Accounts receivable	7,455	6,181
Inventories	9,134	3,000
Prepaid expenses and other	3,841	3,566
Total current assets	171,605	96,299
Noncurrent assets:		
Fixed assets, net	5,880	1,810
Goodwill	3,275	3,275
Intangible assets, net	2,974	3,213
Other assets	5,332	4,129
Total Assets	$189,066	$108,726
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$2,550	$5,264
Accrued liabilities	16,859	13,128
Common stock warrant liability	711	7,066
Deferred revenue	-	4,698
Note payable, current portion	9,000	-
Total current liabilities	29,120	30,156
Noncurrent liabilities:		
Note payable, net of current portion	51,000	50,000
Convertible notes	60,000	-
Total liabilities	140,120	80,156
Stockholders' equity:		
Preferred stock, $0.001 par value per share, 15,000,000 shares authorized, zero shares issued and outstanding	-	-
Common stock, $0.001 par value per share, 150,000,000 shares authorized, 68,861,366 and 61,614,576 shares issued and outstanding at December 31, 2014 and 2013, respectively	69	62
Additional paid-in capital	306,832	234,246
Accumulated other comprehensive loss	(60)	(383)
Accumulated deficit	(257,895)	(205,355)
Total stockholders' equity	48,946	28,570
Total Liabilities and Stockholders' Equity	$189,066	$108,726

The accompanying notes are an integral part of these consolidated financial statements.

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RAPTOR PHARMACEUTICAL CORP.
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(In thousands, except shares and per share data)

	For the Year Ended December 31,		For the Four Months Ended December 31,	For the Year Ended August
	2014	2013	2012	31, 2012
Revenues	$69,497	$16,872	$-	$-
Cost of sales	9,416	1,653	-	-
Gross profit	60,081	15,219	-	-
Operating expenses:				
Research and development	43,477	29,177	8,963	21,443
Selling, general and administrative	56,654	37,948	8,971	14,723
Total operating expenses	100,131	67,125	17,934	36,166
Loss from operations	$(40,050)	$(51,906)	$(17,934)	$(36,166)
Interest income	76	188	160	340
Interest expense	(13,971)	(6,832)	(83)	(3)
Foreign currency transaction gain	261	8	113	145
(Loss) gain on short-term investments	-	(128)	(64)	213
Adjustment to fair value of common stock warrants	(1,148)	(10,747)	(1,484)	(3,173)
Other income	2,346	-	-	-
Net loss before provision for income taxes	(52,486)	(69,417)	(19,292)	(38,644)
Provision for income taxes	(54)	-	-	-
Net Loss	$(52,540)	$(69,417)	$(19,292)	$(38,644)
Other comprehensive income (loss):				
Foreign currency translation gain (loss)	323	(268)	(65)	(52)
Comprehensive Loss	$(52,217)	$(69,685)	$(19,357)	$(38,696)
Net loss per share:				
Basic and diluted	$(0.83)	$(1.20)	$(0.37)	$(0.80)
Weighted-average shares outstanding:				
Basic and diluted	63,213,504	57,860,366	51,736,956	48,084,633

The accompanying notes are an integral part of these consolidated financial statements.

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RAPTOR PHARMACEUTICAL CORP.
CONSOLIDATED STATEMENT OF STOCKHOLDERS' EQUITY (DEFICIT)
(In thousands, except shares and per share data)

	Common Stock		Additional Paid In	Accumulated Other Comprehensive Income	Accumulated	
	Shares	Amount	Capital	(Loss)	Deficit	Total
Balance at August 31, 2011	35,569	$ 36	$73,817	$ 2	$ (78,002)	$(4,147)
Net loss	-	-	-	-	(38,644)	(38,644)
Other comprehensive income (loss)	-	-	-	(52)	-	(52)
Issuance of common stock:						-
Follow-on public offering, net of offering costs	11,500	12	42,822	-	-	42,834
At-the-market financing facility, net of offering costs	1,508	1	7,323	-	-	7,324
Exercise of common stock options	160	-	366	-	-	366
Exercise of common stock warrants	1,831	2	5,011	-	-	5,013
Reclassification of the fair value of warrant liabilities upon exercise	-	-	9,482	-	-	9,482
Stock-based compensation	-	-	4,559	-	-	4,559
Balance at August 31, 2012	50,568	51	143,380	(50)	(116,646)	26,735
Net loss	-	-	-	-	(19,292)	(19,292)
Other comprehensive income (loss)	-	-	-	(65)	-	(65)
Issuance of common stock:						-
At-the-market financing facility, net of offering costs	1,153	1	5,946	-	-	5,947
Exercise of common stock options	79	-	192	-	-	192
Exercise of common stock warrants	625	-	1,843	-	-	1,843
Reclassification of the fair value of warrant liabilities upon exercise			2,345			2,345
Stock-based compensation	-	-	2,239	-	-	2,239
Balance at December 31, 2012	52,425	52	155,945	(115)	(135,938)	19,944
Net loss	-	-	-	-	(69,417)	(69,417)
Other comprehensive income (loss)	-	-	-	(268)	-	(268)
Issuance of common stock:						-
At-the-market financing facility, net of offering costs	4,939	5	38,389	-	-	38,394
Exercise of common stock options	651	1	2,474	-	-	2,475
Exercise of common stock warrants	3,600	4	10,322	-	-	10,326
Reclassification of the fair value of warrant liabilities upon exercise			20,086		-	20,086
Stock-based compensation	-	-	7,030	-	-	7,030
Balance at December 31, 2013	61,615	62	234,246	(383)	(205,355)	28,570
Net loss	-	-	-	-	(52,540)	(52,540)
Other comprehensive income (loss)	-	-	-	323	-	323
Issuance of common stock:						-
Employee stock purchase plan	21	-	179	-	-	179
	4,970	4	44,459	-	-	44,463

At-the-market financing facility, net of offering costs						
Exercise of common stock options	1,643	2	6,574	-	-	6,576
Exercise of common stock warrants	612	1	1,825	-	-	1,826
Reclassification of the fair value of warrant liabilities upon exercise	-	-	7,503	-	-	7,503
Stock-based compensation	-	-	12,046	-	-	12,046
Balance at December 31, 2014	68,861	$ 69	$306,832	$ (60)	$ (257,895)	$48,946

The accompanying notes are an integral part of these consolidated financial statements.

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RAPTOR PHARMACEUTICAL CORP.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(In Thousands)

	For the Year Ended December 31,		For the Four Months Ended December 31,	For the Year Ended August 31,
	2014	2013	2012	2012
Cash flows from operating activities:				
Net loss	$(52,540)	$(69,417)	$(19,292)	$(38,644)
Adjustments to reconcile net loss to net cash used in operating activities:				
Stock-based compensation expense	12,046	7,030	2,239	4,559
Fair value adjustment of common stock warrants	1,148	10,747	1,484	3,173
Amortization of intangible assets	239	193	49	146
Depreciation of fixed assets	798	244	42	65
Realized loss (gain) on disposal of fixed assets	219	(12)	-	-
Loss on short-term investments	-	128	64	-
Write-off of intangible assets and other intellectual property	-	-	-	900
Amortization of debt issuance cost	1,626	433	-	-
Changes in assets and liabilities:				
Accounts receivable	(1,274)	(6,181)	-	-
Inventories	(6,134)	(3,000)	-	-
Prepaid expenses and other assets	572	(2,028)	1,580	(2,695)
Accounts payable	(2,714)	(114)	3,081	754
Accrued liabilities	3,731	10,683	(593)	403
Deferred revenue	(4,698)	4,698	-	(10)
Net cash used in operating activities	(46,981)	(46,596)	(11,346)	(31,349)
Cash flows from investing activities:				
Net purchase of fixed assets	(5,086)	(1,586)	(57)	(385)
Purchase of short-term investments	-	(147)	(6,853)	(45,307)
Sale of short-term investments	-	22,114	-	30,000
Intangible assets	-	(1,250)	-	-
Change in restricted cash	(1,062)	(337)	6	(54)
Net cash (used in) provided by investing activities	(6,148)	18,794	(6,904)	(15,746)
Cash flows from financing activities:				
Proceeds from sale of common stock, net	-	-	-	42,834
Proceeds from sale of common stock under ATM agreement	44,463	38,394	5,947	7,324
Proceeds from the exercise of common stock warrants	1,826	10,326	1,843	5,013
Proceeds from the exercise of common stock options and ESPP	6,755	2,475	192	366
Proceeds from issuance of debt	70,000	25,000	25,000	-
Debt issuance costs	(3,521)	(1,260)	(1,959)	-
Offering costs	(156)	(126)	25	18
Net cash provided by financing activities	119,367	74,809	31,048	55,555
Effect of exchange rates on cash and cash equivalents	323	(268)	(65)	(52)

Net increase in cash and cash equivalents	66,561	46,739	12,733	8,408
Cash and cash equivalents, beginning of period	83,052	36,313	23,580	15,172
Cash and Cash Equivalents, End of Period	$149,613	$83,052	$ 36,313	$23,580
Supplemental cash flow information:				
Interest paid	$11,654	$5,412	$ 83	$3
Income taxes paid	$176	$2	$ -	$-
Supplemental disclosure of non-cash financing activities:				
Fair value of warrant liability reclassified to equity upon exercise	$7,503	$20,086	$ 2,345	$9,482

The accompanying notes are an integral part of these consolidated financial statements.

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RAPTOR PHARMACEUTICAL CORP.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
December 31, 2014

1. NATURE OF OPERATIONS AND BUSINESS RISKS

The accompanying consolidated financial statements reflect the financial position and results of operations of Raptor Pharmaceutical Corp. (the "Company" or "Raptor") and have been prepared in accordance with the accounting principles generally accepted in the United States of America ("GAAP").

Raptor is a biopharmaceutical company focused on developing and commercializing life-altering therapeutics that treat debilitating and often fatal diseases. The Company's first product, PROCYSBI® (cysteamine bitartrate) delayed-release capsules ("PROCYSBI"), received marketing approval from the U.S. Food and Drug Administration ("FDA") on April 30, 2013 for the management of nephropathic cystinosis in adults and children six years and older. In Europe, PROCYSBI® gastro-resistant hard capsules of cysteamine (as mercaptamine bitartrate), received marketing authorization on September 6, 2013 from the European Commission ("EC"), for marketing in the European Union ("EU") as an orphan medicinal product for the management of proven nephropathic cystinosis. PROCYSBI received seven years of market exclusivity as an orphan drug in the United States and ten years of market exclusivity as an orphan drug in the EU. The Company commenced commercial sales of PROCYSBI in the United States in mid-June 2013, in Europe in April 2014. For at least the near term, the Company's ability to generate revenues is entirely dependent upon sales of PROCYSBI in the United States for the management of nephropathic cystinosis in adults and children six years and older and in the EU for the management of proven nephropathic cystinosis.

Raptor's pipeline includes its proprietary delayed-release form of cysteamine, or RP103 and its proprietary oral 4-methylpyrazole, or Convivia™. Raptor currently has product candidates in clinical development designed to potentially treat Huntington's disease ("HD"), non-alcoholic steatohepatitis ("NASH") in children, Leigh syndrome and other mitochondrial disorders and aldehyde dehydrogenase deficiency ("ALDH2"). Raptor's preclinical programs are based upon bioengineered novel drug candidates that are designed to target cancer and other diseases.

The Company is subject to a number of risks, including: the level of commercial sales of PROCYSBI in the United States and Europe; the ability to successfully launch PROCYSBI in other international markets; uncertainty whether the Company's research and development efforts will result in expanded labeling for PROCYSBI and commercialization for RP103 in various indications or additional commercial products; competition from other organizations; reliance on licensing the proprietary technology of others; uncertain patent protection; and the need to raise capital through equity and/or debt financings. Funding may not be available when needed if at all or on terms acceptable to the Company. If the Company exhausts its cash reserves and is unable to obtain adequate financing, it may be required to curtail planned operating expenditures, including its development programs.

Change in Fiscal Year End

On December 4, 2012, Raptor's Board of Directors approved a change in its fiscal year end from August 31 to December 31. The change became effective at the end of the four months ended December 31, 2012. All references to "fiscal years" or "years" prior to this change refer to the twelve-month fiscal period covering September 1 through August 31, and each year after December 31, 2012, the fiscal year covers January 1 through December 31.

Basis of Presentation

The Company's consolidated financial statements include the accounts of the Company's direct and indirect wholly owned subsidiaries, Raptor Pharmaceuticals Inc., formerly known as Raptor Therapeutics Inc. which merged with Raptor Discoveries Inc. in December 2012 prior to changing its name, and Raptor European Products, LLC, such

subsidiaries incorporated in Delaware on August 1, 2007, and February 14, 2012, respectively, and Raptor Pharmaceuticals Europe B.V. (“BV”), Raptor Pharmaceuticals France SAS (“SAS”), Raptor Pharmaceuticals Germany GmbH (“GMBH”) and RPTP European Holdings C.V. (“CV”), domiciled in the Netherlands on December 15, 2009, in France on October 30, 2012, in Germany on October 16, 2013 and in the Cayman Islands on February 16, 2012, respectively. All inter-company accounts have been eliminated. Net assets in foreign countries totaled $5.8 million at December 31, 2014.

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2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make certain estimates and assumptions that affect the reported amounts of assets and liabilities, disclosure of contingent assets and liabilities as of the dates of the consolidated financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates.

Functional Currency

The Company's consolidated functional currency is the U.S. dollar. BV, SAS, and GMBH, the Company's Dutch subsidiary, French subsidiary, and German Subsidiary, respectively, use the European Euro as their functional currency. The CV subsidiary, a Cayman-based subsidiary, uses the dollar as its functional currency. At each quarter end, each foreign subsidiary's balance sheets are translated into U.S. dollars based upon the quarter-end exchange rate, while their statements of operations and comprehensive loss are translated into U.S. dollars based upon an average exchange rate during the period.

Segment Information

The Company has determined that it operates in only one segment, as it only reports profit and loss information on an aggregate basis to its chief operating decision maker. The Company's long-lived assets maintained outside the United States are not material.

Fair Value of Financial Instruments

The carrying amounts of certain of the Company's financial instruments including cash equivalents, restricted cash, accounts payable, accrued liabilities, note payable and capital lease liability approximate fair value due either to length of maturity or interest rates that approximate prevailing market rates. The warrant liability is carried at fair value, which is determined using the Black-Scholes option valuation model at the end of each reporting period.

Cash and Cash Equivalents

The Company considers all highly liquid investments with original maturities of three months or less, when purchased, to be cash equivalents. The Company maintains cash and cash equivalents, which consist principally of money market funds, with high credit quality financial institutions. Such amounts exceed Federal Deposit Insurance Corporation insurance limits. Restricted cash represents certificates of deposit and compensating balances required by the Company's U.S. and European banks as collateral for credit cards and for access to a value-added tax deferral program. As of December 31, 2014, the Company had $149.6 million in cash and cash equivalents, of which $5.4 million was held by its foreign subsidiaries.

Revenue Recognition and Accounts Receivable

The Company recognizes revenue in accordance with the Financial Accounting Standards Board ("FASB") Accounting Standards Codification (“ASC”) 605, Revenue Recognition, when the following criteria have been met: persuasive evidence of an arrangement exists; delivery has occurred and risk of loss has passed; the seller's price to the

buyer is fixed or determinable and collectability is reasonably assured. The Company determines that persuasive evidence of an arrangement exists based on written contracts that define the terms of the arrangements. Pursuant to the contract terms, the Company determines when title to products and associated risk of loss has passed on to the customer. The Company assesses whether the fee is fixed or determinable based on the payment terms associated with the transaction and whether the sales price is subject to refund or adjustment. The Company assesses collectability based primarily on the customer's payment history and creditworthiness.

PROCYSBI is currently available for U.S. distribution from the Company's U.S. specialty pharmacy partner, the Accredo Health Group, Inc. ("Accredo") which is currently the Company's only U.S. customer and ships directly to patients. The Company's distributor in the EU is the Almac Group, Ltd. PROCYSBI is not available in U.S. retail pharmacies. Prior authorization of coverage by patients' commercial insurance plans, Raptor's patient assistance program ("PAP") or government payors is a prerequisite to the shipment of PROCYSBI to U.S. patients. Prior to the third quarter of 2014, revenue was recognized in the United States once the product had been shipped by the specialty pharmacy to patients because the Company had not yet been able to reasonably estimate the third-party payor mix and resulting rebates based on its lack of sufficient historical data. Beginning July 2014, the Company was able to reasonably estimate and determine sales allowances; therefore the Company began recognizing PROCYSBI revenue at the point of sale to the specialty pharmacy, which resulted in the one-time non-recurring recognition of an additional $4.4 million in net revenues during the quarter ended September 30, 2014. Revenue is currently recognized in the EU once confirmed orders from the pharmacies have been shipped and invoiced for payment by the distributor on the Company’s behalf.

The Company records revenue net of expected discounts, distributor fees, and rebates, including government rebates such as Medicare and Medicaid in the United States. Allowances are recorded as a reduction of revenue at the time product sales are recognized. Allowances for government rebates and discounts are established based on the actual payor and payor mix information, which is known in the United States at the time of shipment to the distributor and in Germany at the time of shipment to the pharmacy, and the government-mandated discount rates applicable to government-funded programs. The allowances are adjusted to reflect known changes in the factors that may impact such allowances in the quarter the changes are known.

Trade accounts receivable are recorded net of product sales allowances for prompt-payment discounts and chargebacks. Estimates for chargebacks and prompt-payment discounts are based on contractual terms and the Company's expectations regarding the utilization rates.

Inventories and Cost of Sales

Inventories are stated at the lower of cost or market price, with cost determined on a first-in, first-out basis. Inventories are reviewed periodically to identify slow-moving inventory based on sales activity, both projected and historical, as well as product shelf-life. Prior to the approval of PROCYSBI by the FDA on April 30, 2013 and in Europe, prior to the approval by the EC on September 6, 2013, the Company recorded the purchase of raw materials and the manufacturing costs relating to PROCYSBI as research and development expense. Subsequent to FDA and EC approval, the Company began capitalizing these costs and manufacturing overhead as commercial inventory. Upon launching PROCYSBI in mid-June 2013 in the United States and April 2014 in the EU, the Company began recognizing cost of sales. Cost of sales includes the cost of inventory sold or reserved; manufacturing, manufacturing overhead and supply chain costs; product shipping and handling costs; and amortization of licensing approval milestone payments and licensing royalties payable to the University of California, San Diego ("UCSD").

Prepaid Expenses and Other

Prepaid expenses consists primarily of advance vendor payments which will be expensed within one year from the balance sheet date, including $0.5 million prepaid to the National Institute of Diabetes and Digestive and Kidney Diseases (“NIDDK”) which is part of the National Institutes of Health. Such amounts relate to a clinical trial being conducted under a Cooperative Research and Development Agreement (“CRADA”) with the NIDDK, and are being recorded to research and development expense over the estimated term of the trial. See Note 13 for additional

information on future payments due under the CRADA. Other assets consist primarily of amounts receivable for vendor refunds, stock option exercises, and VAT tax refunds, including $0.7 million from Cambrex for API purchase refunds and $0.2 million from the FDA for PDUFA filing fee refunds.

Fixed Assets

Fixed assets, which mainly consist of leasehold improvements, office furniture, lab equipment and computer hardware and software, are stated at cost. Depreciation is computed using the straight-line method over the related estimated useful lives, except for leasehold improvements and capital lease equipment, which are depreciated over the shorter of the useful life of the asset or the lease term. Significant additions and improvements that have useful lives estimated at greater than one year are capitalized, while repairs and maintenance are charged to expense as incurred.

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Goodwill and Intangible Assets

Intangible assets primarily include the intellectual property and other rights relating to DR Cysteamine (currently developed as RP103) and to an out-license acquired in a 2009 merger. The intangible assets related to RP103 are amortized using the straight-line method over the estimated useful life of 20 years, which is the life of the intellectual property patents. The 20-year estimated useful life is also based upon the typical development, approval, marketing and life cycle management timelines of pharmaceutical drug products.

Goodwill represents the excess of the purchase price over the fair value of tangible and identified intangible net assets of businesses acquired. Goodwill is not amortized, but is evaluated for impairment on an annual basis or more often when impairment indicators are present. The Company has one reporting unit. Therefore, the Company's consolidated net assets, including existing goodwill and other intangible assets, are considered to be the carrying value of the reporting unit. If the carrying value of the reporting unit is in excess of its fair value, an impairment may exist, and the Company must perform the second step of the analysis, in which the implied fair value of the goodwill is compared to its carrying value to determine the impairment charge, if any. If the estimated fair value of the reporting unit exceeds the carrying value of the reporting unit, goodwill is not impaired and no further analysis is required.

The Company makes judgments about the recoverability of purchased intangible assets with finite lives whenever events or changes in circumstances indicate that impairment may exist. Recoverability of purchased intangible assets with finite lives is measured by comparing the carrying amount of the asset to the future undiscounted cash flows the asset is expected to generate. Impairment, if any, is measured as the amount by which the carrying value exceeds the fair value of the impaired asset.

Common Stock Warrant Liabilities

The Company issued warrants that contain conditional obligations that may require the Company to transfer cash to settle the warrants upon the occurrence of certain fundamental transactions. Therefore, the Company has classified the warrants as liabilities. The Company re-measures the liability at the end of every reporting period with the change in value reported in the Company's consolidated statements of operations and comprehensive loss. At the exercise date, the fair values of these warrants are re-measured and reclassified to equity.

Note Payable

Note payable consists of a loan agreement with HealthCare Royalty Partners II, L.P. ("HC Royalty"), as lender, which was amended effective July 1, 2014. The amendment qualified as a modification of debt in accordance with ASC 470-50, Debt – Modifications and Extinguishments, as the Company determined it did not result in substantially different terms. The amended loan requires quarterly interest payments at an annual fixed interest rate of 8.0% of outstanding principal and includes a synthetic royalty component based on net product sales, including PROCYSBI, in a calendar year. The amended loan is a senior secured obligation of the Company.

Note payable is carried at its unpaid principal balance. The fixed and royalty interest under both agreements were recognized as interest expense as incurred.

Convertible Notes

Convertible notes include unsecured convertible senior notes and are carried at their unpaid principal balance. Interest on the notes is payable quarterly and the notes mature on August 1, 2019. If converted by a holder, upon conversion, the holder of the notes would receive shares of the Company’s common stock.

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Debt Issuance Costs

Debt issuance costs are expenses associated with the issuance of the loan agreements with HC Royalty and the convertible notes. Debt issuance costs which were capitalized are being amortized over the life of the respective debt to interest expense using the interest method. Debt issuance costs are a component of Other Assets on the Company's consolidated balance sheets.

Other Income

In 2014, we recorded other income of $2.3 million related to disgorgement of alleged short-swing profits under Section 16(b) of the Securities Exchange Act of 1934 from a stockholder. This amount is recorded as Other Income on the Company’s consolidated financial statements.

Net Loss per Share

Net loss per share is calculated by dividing net loss by the weighted-average shares of common stock outstanding during the period. Diluted net loss per share is calculated by dividing net loss by the weighted-average shares of common stock outstanding and potential shares of common stock during the period. For all periods presented, potentially dilutive securities are excluded from the computation of fully diluted net loss per share as their effect is anti-dilutive. Potentially dilutive securities include:

	Year Ended December 31,		For the Four Months Ended December 31,	For the Year Ended August 31,
	2014	2013	2012	2012
Warrants to purchase common stock	334,764	946,370	4,562,772	5,187,772
Options to purchase common stock	8,857,961	8,217,674	7,790,794	6,124,823
Convertible debt	3,428,571	-	-	-
Total Potentially Dilutive Securities	12,621,296	9,164,044	12,353,566	11,312,595

Comprehensive Loss

The components of comprehensive loss include net loss and foreign currency translation adjustments.

Stock-Based Compensation

Stock Option Plan

Compensation costs related to the Company's stock option plan are measured at the grant date based on the fair value of the equity instruments awarded and are recognized over the period during which an employee is required to provide service in exchange for the award, or the requisite service period, which is usually the vesting period. The compensation expense for stock-based compensation awards is reduced by an estimate for forfeitures.

The Company recognizes expense associated with stock options issued to third parties, including consultants, based upon the fair value of such awards on the date the options vest.

Employee Stock Purchase Plan

In July 2014, the Company's shareholders approved the Raptor Pharmaceutical Corp. 2013 Employee Stock Purchase Plan ("ESPP"). Up to 1,000,000 shares may be issued pursuant to the ESPP. The purpose of the ESPP is to give the Company's employees an opportunity to acquire an equity interest in the Company through the purchase of shares of common stock at a discount. The ESPP allows eligible employees to purchase common stock at 85% of its fair value, subject to certain limits. Fair value as defined under the ESPP is the lesser of the closing market price of the common stock on the first day of the offering period or the last day of the offering period, which is a six-month period beginning on each May 15 and November 15.

Research and Development

Research and development costs are charged to expense as incurred. Research and development expenses primarily include salaries and benefits for medical, clinical, regulatory, quality, pharmacovigilance and research personnel, preclinical studies, clinical trials, and certain commercial drug manufacturing expenses prior to obtaining marketing approval.

Advertising Expenses

The Company expenses advertising costs, including promotional expenses, as incurred. For the years ended December 31, 2014 and 2013, the four months ended December 31, 2012 and the fiscal year ended August 31, 2012, advertising expenses were $1.4 million, $3.7 million, $1.3 million and $0.6 million, respectively.

Income Taxes

Income taxes are recorded under the liability method, under which deferred tax assets and liabilities are determined based on the difference between the financial statement and tax bases of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to affect taxable income. Valuation allowances are established when necessary to reduce deferred tax assets to the amount expected to be realized. Based on the weight of available evidence, including cumulative losses since inception and expected future losses, the Company has determined that it is more likely than not that the deferred tax asset amount will not be realized and therefore a full valuation allowance has been provided on the Company's net deferred tax assets.

The Company identifies uncertain tax positions and discloses any potential tax liability on its financial statements. The Company recognizes interest and/or penalties related to income tax matters as a component of income tax expense. As of December 31, 2014, there were no accrued uncertain tax positions or interest and penalties related to uncertain tax positions.

The Company files U.S. Federal, California, various other state and other income tax returns and various foreign country income tax returns. The Company is currently not subject to any income tax examinations. Due to the Company's net operating losses ("NOLs"), generally all tax years remain open.

Reclassifications

Certain amounts previously reported under specific financial statement captions have been reclassified to be consistent with the current period presentation.

Recent Accounting Pronouncements

In May 2014, the FASB issued Accounting Standards Update (“ASU”) 2014-09, Revenue from Contracts with Customers, which outlines a single comprehensive model for entities to use in accounting for revenue arising from contracts with customers and supersedes most current revenue recognition guidance, including industry-specific guidance. The core principle of the revenue model is that “an entity recognizes revenue to depict the transfer of promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services.” In applying the revenue model to contracts within its scope, the Company will: identify the contract(s) with a customer, identify the performance obligations in the contract, determine

the transaction price, allocate the transaction price to the performance obligations in the contract, and recognize revenue when (or as) the entity satisfies a performance obligation. This ASU is effective for interim and annual periods beginning after December 15, 2016 and early adoption is not permitted. The Company does not believe the adoption of this ASU will have a material impact on its consolidated financial statements.

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In June 2014, the FASB issued ASU 2014-12, Accounting for Share-Based Payments When the Terms of an Award Provide That a Performance Target Could Be Achieved after the Requisite Service Period. The ASU requires that a performance target that affects vesting, and that could be achieved after the requisite service period, be treated as a performance condition. A reporting entity should apply existing guidance in Topic 718 as it relates to awards with performance conditions that affect vesting to account for such awards. This ASU is effective for interim and annual periods beginning after December 15, 2015 and early adoption is permitted. The Company does not anticipate the adoption of this ASU will have a material impact on its consolidated financial statements.

In August 2014, the FASB issued ASU No. 2014-15, Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern, which provides guidance on determining when and how reporting entities must disclose going-concern uncertainties in their financial statements. The ASU requires management to perform interim and annual assessments of an entity's ability to continue as a going concern within one year of the date of issuance of the entity's financial statements (or within one year after the date on which the financial statements are available to be issued, when applicable). Further, an entity must provide certain disclosures if there is "substantial doubt about the entity's ability to continue as a going concern." This ASU is effective for annual periods ending after December 15, 2016, and interim periods thereafter; early adoption is permitted.

3. FAIR VALUE MEASUREMENT

The Company uses a fair value approach to value certain assets and liabilities. Fair value is the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or liability. The Company uses a fair value hierarchy, which distinguishes between assumptions based on market data (observable inputs) and an entity's own assumptions (unobservable inputs). The hierarchy consists of three levels:

- Level 1 –Quoted market prices in active markets for identical assets or liabilities;
- Level 2 –Inputs other than level one inputs that are either directly or indirectly observable; and
- Level 3 –Unobservable inputs developed using estimates and assumptions, which are developed by the reporting entity and reflect those assumptions that a market participant would use.

Determining which category an asset or liability falls within the hierarchy requires significant judgment. The Company evaluates its hierarchy disclosures each reporting period. The following table presents the assets and liabilities recorded that are reported at fair value on our consolidated balance sheets on a recurring basis.

Assets and Liabilities Measured at Fair Value on a Recurring Basis

(In thousands)

December 31, 2014	Level 1	Level 2	Level 3	Total
Assets				
Cash equivalents [1]	$137,938	$ -	$-	$137,938
Total	$137,938	$ -	$-	$137,938
Liabilities				
Common stock warrants	$-	$ -	$711	$711

Total	$-	$ -	$711	$711

December 31, 2013	Level 1	Level 2	Level 3	Total
Assets				
Cash equivalents [1]	$70,627	$ -	$-	$70,627
Total	$70,627	$ -	$-	$70,627
Liabilities				
Common stock warrants	$-	$ -	$7,066	$7,066
Total	$-	$ -	$7,066	$7,066

(1) Cash equivalents represent the fair value of the Company's investments in money market funds at December 31, 2014 and 2013.

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Certain of the Company's common stock warrants are classified as liabilities and are, therefore, re-measured using the Black-Scholes option valuation model at the end of each reporting period with the change in value reported in the Company's consolidated statements of operations and comprehensive loss.

The following table presents a reconciliation of the Company's recurring fair value measurements categorized within Level 3 of the fair value hierarchy (liability-classified common stock warrants).

Changes in Level 3 Liabilities Measured at Fair Value on a Recurring Basis – Common Stock Warrants

	Year Ended December 31,		For the Four Months Ended December 31,	For the Year Ended August 31,
(In thousands)	2014	2013	2012	2012
Beginning fair value	$7,066	$16,405	$ 17,266	$23,575
Change in fair value recognized in earnings	1,148	10,747	1,484	3,173
Exercises	(7,503)	(20,086)	(2,345)	(9,482)
Ending Fair Value	$711	$7,066	$ 16,405	$17,266

Effect of Raptor's Stock Price and Volatility Assumptions on the Calculation of Fair Value of Warrant Liabilities

As discussed above, the Company uses the Black-Scholes option pricing model as its method of valuation for warrants that are subject to warrant liability accounting. The determination of fair value as of the reporting date is affected by Raptor's stock price as well as assumptions regarding a number of subjective variables. These variables include, but are not limited to, expected stock price volatility over the term of the security and risk-free interest rate. The primary factors affecting the fair value of the warrant liability are the Company's stock price and volatility.

The following table presents the carrying value and fair value of certain financial liabilities that are recorded on the Company’s consolidated balance sheets.

Fair Value of Certain Financial Liabilities

(In thousands)	Carrying	Fair
December 31, 2014	Value	Value
Liabilities		
Note payable	$60,000	$65,522
Convertible notes	60,000	56,760

4. INVENTORIES

Inventories consist of raw materials, work-in-process and finished goods related to the manufacture of PROCYSBI. Raw materials include the Company's active pharmaceutical ingredient ("API"), cysteamine bitartrate.
Work-in-process includes third party manufacturing and associated labor costs relating to the Company's personnel directly involved in the production process. Also included in inventories are raw materials that may be used for

clinical trials, which are charged to research and development (“R&D”) expense when consumed.

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Inventories are summarized as follows:

	December 31,	
(In thousands)	2014	2013
Raw materials	$6,290	$2,469
Work-in-process	721	-
Finished goods	2,123	531
Total Inventories	$9,134	$3,000

5. FIXED ASSETS

Fixed assets consisted of:

	December 31,		Estimated useful
(In thousands)	2014	2013	lives
Assets under construction	$2,393	$102	-
Office furniture	2,198	605	7 years
Laboratory equipment	1,373	1,132	5 years
Computer hardware and software	815	646	3 years
Leasehold improvements	470	-	Lease term
Total at cost	7,249	2,485	
Less: accumulated depreciation	(1,369)	(675)	
Total Fixed Assets, Net	$5,880	$1,810	

Depreciation expense for the years ended December 31, 2014 and 2013, the four months ended December 31, 2012 and the year ended August 31, 2012 was $798 thousand, $244 thousand, $42 thousand, and $65 thousand, respectively.

6. INTANGIBLE ASSETS AND GOODWILL

On December 14, 2007, the Company acquired the intellectual property and other rights to develop RP103 to treat various clinical indications from UCSD by way of a merger with Encode Pharmaceuticals, Inc., a privately held development stage company ("Encode"), which held the intellectual property license with UCSD. The fair value of the intangible assets at the time of acquisition was approximately $2.6 million.

Pursuant to the license agreement with UCSD, the Company is obligated to pay milestone payments upon the occurrence of certain events, royalties on net sales from products developed pursuant to the license agreement and a percentage of sublicense fees or royalties, if any. The Company is obligated to fulfill predetermined milestones within a specified number of years from the effective date of the license agreement, depending on the indication. To the extent that the Company fails to perform any of its obligations under the agreement, UCSD may terminate the license or otherwise cause the license to become non-exclusive.

In May 2013, the Company announced that the FDA has approved PROCYSBI (cysteamine bitartrate) delayed release capsules for the management of nephropathic cystinosis in adults and children 6 years and older. Subsequently, the

Company announced that the EC has approved PROCYSBI® gastro-resistant hard capsules of cysteamine (as mercaptamine bitartrate) as an orphan medicinal product for the management of proven nephropathic cystinosis for marketing in the EU. In conjunction with these approvals, the Company paid milestone payments to UCSD during the second and third quarters of 2013 of $0.8 million and $0.5 million, respectively, pursuant to this license, which were capitalized as intangible assets.

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A summary of intangibles acquired is as follows:

(In thousands)	Useful Life (Years)	December 31, 2014	2013
Intangible asset (IP license for RP103) related to the Encode merger	20.0	$2,620	$2,620
Intangible assets (UCSD license - FDA and EC approval milestones)	20.0	1,250	1,250
Other intangible assets	16.0	240	240
Total intangible assets		4,110	4,110
Less accumulated amortization		(1,136)	(897)
Intangible Assets, Net		$2,974	$3,213

The intangible assets related to RP103 are being amortized over an estimated useful life of 20 years, which is the life of the intellectual property patents. The 20 year estimated useful life is also based upon the typical development, approval, marketing and life cycle management timelines of pharmaceutical drug products. Other intangible assets are being amortized using the straight-line method over an estimated useful life of 16 years, which is the life of the intellectual property patents.

As of August 31, 2012, the Company had determined that its acquired in-process research and development asset was impaired and wrote off the $0.9 million carrying amount to research and development expense. During the years ended December 31, 2014 and 2013, and the four months ended December 31, 2012, there was no intangible asset impairment recognized.

During the years ended December 31, 2014 and 2013, the four months ended December 31, 2012 and the fiscal year ended August 31, 2012, the Company amortized $239 thousand, $193 thousand, $49 thousand, and $146 thousand, respectively, of intangible assets.

Amortization expense for intangible assets for each of the next five years is as follows:

(In thousands)	Amortization Expense
2015	$ 238
2016	238
2017	238
2018	238
2019	238

The Company tested the carrying value of goodwill for impairment as of December 31, 2014 and determined that there was no impairment.

7. ACCRUED LIABILITIES

Accrued liabilities consisted of:

(In thousands)	December 31, 2014	2013

Personnel-related costs	$6,879	$4,443
Rebates and other sales deductions	3,231	2,325
Clinical trials and research and development costs	2,522	1,661
License royalty payable	972	564
Royalty-based interest payable	369	1,255
Manufacturing costs	284	294
Other	2,602	2,586
Total Accrued Liabilities	$16,859	$13,128

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8. NOTE PAYABLE

On December 20, 2012, the Company entered into a loan agreement with HC Royalty, as lender, under which it agreed to borrow $50.0 million in two $25.0 million tranches. The Company received $23.4 million in net proceeds from the first tranche of the loan at closing in December 2012 and an additional $23.7 million in net proceeds in May 2013 from the second tranche upon FDA approval of PROCYSBI.

In July 2014, the Company entered into an amended and restated loan agreement with HC Royalty which revised the terms of the 2012 loan agreement between the Company and HC Royalty, and also provided for an additional $10 million in term loan funding. The interest rate was revised to an annual fixed rate of 8.0%, compared to the original interest rate of 10.75%. The loan also contains a synthetic royalty component based on net product revenues, including PROCYSBI, in a calendar year, and such royalty is payable quarterly. The variable royalty rate under the amended and restated loan agreement has been revised to 8.0% on the first $50 million of revenue and 2.0% on revenue in excess of $50 million. The first quarterly principal payment of $3 million is due in June 2015. All term loans under the amended and restated loan agreement mature on March 31, 2020. The loan and the Company's obligation to make payments thereunder shall terminate immediately when all payments received by HC Royalty equal $120.0 million.

Prior to July 1, 2014, with respect to the first $25.0 million tranche, for each calendar year (prorated for any portion thereof), the loan bore a royalty rate of 6.25% of the first $25.0 million of product net revenues, 3.0% of product net revenues for such calendar year in excess of $25.0 million and up to $50.0 million, and 1.0% of product net revenues for such calendar year in excess of $50.0 million, payable quarterly. Prior to July 1, 2014, with respect to the second $25.0 million tranche, for each calendar year (prorated for any portion thereof), the loan bore a royalty rate of 6.0% of the first $25.0 million of net product revenues for such calendar year, 3.0% of product net revenues for such calendar year in excess of $25.0 million and up to $50.0 million, and 1.0% of product net revenues for such calendar year in excess of $50.0 million, payable quarterly.

The Company's amended and restated loan agreement with HC Royalty includes affirmative and negative covenants, including the use of commercially reasonable efforts to exploit RP103 in specific markets and compliance with laws, as well as restrictions on mergers and sales of assets, incurrence of liens, incurrence of indebtedness and transactions with affiliates and other requirements. To secure the performance of the Company's obligations under the loan, the Company granted a security interest to HC Royalty in substantially all of its assets, the assets of its domestic subsidiaries and a pledge of stock of certain of its domestic subsidiaries. The Company's failure to comply with the terms of the loan and related documents, the occurrence of a change of control of the Company or the occurrence of an uncured material adverse effect on the Company or the occurrence of certain other specified events, will result in an event of default under the loan that, if not cured or waived, could result in the acceleration of the payment of all of its indebtedness, as well as prepayment penalties, to HC Royalty and interest thereon. Under the terms of the security agreement, in an event of default, the lender can potentially take possession of, foreclose on, sell, assign or grant a license to use, the Company's pledged collateral and assign and transfer the pledged stock of certain of its subsidiaries.

The Company received marketing approval of PROCYSBI from the FDA on April 30, 2013 and commenced shipment of PROCYSBI during June 2013, and as a result, royalties became payable to HC Royalty based upon net revenues of PROCYSBI. Interest expense on the loan, excluding amortization of debt issuance costs, for the years ended December 31, 2014 and 2013 and the four months ended December 31, 2012 was approximately $10.6 million, $6.8 million and $0.1 million, respectively.

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The following table presents contractual principal payments of the note payable at December 31, 2014.

(In thousands)	Note Principal Payments
2015	$ 9,000
2016	12,000
2017	12,000
2018	12,000
2019	12,000
2020 and thereafter	3,000
Total	$ 60,000

Unamortized debt issuance costs on the loan agreement totaled $2.3 million and $2.8 million at December 31, 2014 and 2013, respectively. Amortization expense was $1.0 million and $0.4 million for the years ended December 31, 2014 and 2013, respectively, and a nominal amount for the four months ended December 31, 2012.

9. CONVERTIBLE NOTES

In July 2014, the Company sold $60 million aggregate principal amount of 8.0% convertible senior notes due 2019 to HC Royalty and other purchasers. These convertible notes require quarterly interest distributions at a fixed coupon rate equal to 8.0% until maturity or conversion, which will be no later than August 1, 2019. The convertible senior notes are convertible at the option of the holder at a conversion rate of 57.14 common shares per $1,000 principal amount of convertible senior notes at issuance (equivalent to a conversion price of $17.50 per common share), subject to adjustment in certain events. Upon conversion of these convertible senior notes by a holder, the holder will receive shares of the Company’s common stock.

In addition, the Company may elect to exercise the optional redemption, as defined in the note purchase agreement, in which case the convertible senior notes will convert into shares of common stock if the price of the common stock is at or above 175% of the applicable conversion price over a 30 consecutive day period. Upon the occurrence of a “change of control”, as defined in the note purchase agreement, the holders may require the Company to repurchase all or a portion of the notes for cash at 100% of the principal amount of the notes being purchased, plus a repayment premium and any accrued and unpaid interest. To secure the performance of the Company's obligations under the convertible notes agreement, the Company has assigned certain of its assets as collateral.

Interest expense on convertible notes, excluding amortization of debt issuance costs, was $2.1 million for the year ended December 31, 2014. Unamortized debt issuance costs on these convertible notes totaled $2.8 million at December 31, 2014. Amortization expense for the year ended December 31, 2014 was $0.2 million.

10. CAPITAL STRUCTURE

Preferred Stock

At December 31, 2014, the Company was authorized to issue 15,000,000 shares of $0.001 par value per share of preferred stock. There were no shares issued and outstanding.

Common Stock

At December 31, 2014, the Company was authorized to issue 150,000,000 shares of $0.001 par value per share of common stock. Each holder of common stock is entitled to vote on all matters and is entitled to one vote for each share held. As of December 31, 2014 and 2013, there were 68,861,366 and 61,614,576 shares, respectively, of the Company's common stock issued and outstanding.

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Stockholder Rights Plan

The Company's stockholder rights plan entitles the holder of each outstanding share of common stock of the Company to one stock purchase right (a "Right"). Each Right entitles the registered holder to purchase from the Company one thousandth of a share of the Company's Series A Participating Preferred Stock (the "Preferred Shares") at a price of $15 per one one-thousandth of a Preferred Share (the "Purchase Price"), once the Rights become exercisable. The Rights will not be exercisable until the earlier of either (a) 10 days after the public announcement that a person, together with all affiliates or associates of such person, has become an "Acquiring Person" by obtaining beneficial ownership of 15% or more of the Company's outstanding common stock, or (b) 10 business days (or a later date determined by the Board before any person or group becomes an Acquiring Person) after a person or group of affiliated or associated persons begins a tender or exchange offer which, if completed, would result in that person or group of affiliated or associated persons becoming an Acquiring Person. Each one one-thousandth of a share preferred stock, if issued, will have the same voting power as one one-hundred thirty-sixth ($1/136^{th}$) of a share of common stock and will entitle holders to a per share payment equal to the payment made on one one-hundred thirty-sixth ($1/136^{th}$) of a share of common stock, so that one full share of preferred stock would be entitled to receive a payment one one-hundred thirty-sixth (1/136th) of 1,000 times the per share payment to a share of common stock, provided that shares of the Company's common stock are exchanged via merger, consolidation or a similar transaction. The Rights will expire on May 13, 2015 or on an earlier date if the Company redeems or exchanges the Rights.

Common Stock and Warrants Issuance in Connection with the Sale of Units in a Private Placement

On August 21, 2009, Raptor entered into a securities purchase agreement pursuant to which the Company issued shares and warrants for aggregate gross proceeds of approximately $2.4 million. All warrants issued in connection with the August 2009 private placement have been exercised or expired as of December 31, 2014.

2009 Merger and NASDAQ Listing

On September 29, 2009, the Company, formerly known as TorreyPines Therapeutics, Inc. ("TorreyPines") and Raptor Pharmaceutical Corp. ("RPC") completed a reverse merger. The Company changed its name to "Raptor Pharmaceutical Corp." and commenced trading on September 30, 2009 on the NASDAQ Capital Market under the ticker symbol "RPTP". Effective February 29, 2012, the Company's common stock commenced trading on the NASDAQ Global Market. In connection with the merger, the Company assumed all of the TorreyPines stock options and warrants outstanding at the time of the merger. The remaining warrants outstanding are exercisable at $157.08 per share and expire on September 26, 2015.

Common Stock and Warrants Issuance in Connection with the Sale of Units in a Registered Direct Offering

On December 17, 2009, the Company entered into a Placement Agent Agreement (the "2009 Placement Agent"), pursuant to a registered direct offering (the "Direct Offering") of up to 3,748 units (the "Units"), consisting of (i) 3,748 shares of the Company's common stock, (ii) warrants to purchase an aggregate of up to 1,874 shares of the Company's common stock (and the shares of common stock issuable from time to time upon exercise of such warrants) (the "Series A Warrants"), and (iii) warrants to purchase an aggregate of up to 1,874 shares of the Company's common stock (and the shares of common stock issuable from time to time upon exercise of such warrants) (the "Series B Warrants," and collectively with the Series A Warrants, the "Investor Warrants"). All warrants issued in connection with the December 2009 direct offering have been exercised or expired as of December 31, 2014.

Common Stock Issuance in Connection with an Equity Line

On April 16, 2010, the Company signed a purchase agreement with Lincoln Park Capital Fund, LLC ("LPC"), together with a registration rights agreement, whereby LPC agreed to purchase up to $15.0 million of the Company's common stock over a 25 month period.

The purchase price of the shares issued to LPC under the purchase agreement was based on the prevailing market prices of the Company's shares at the time of sale without any fixed discount. The Company controlled the timing and amount of any sales of shares to LPC. LPC did not have the right or the obligation to purchase any shares of the Company's common stock on any business day that the purchase price of the Company's common stock was below $1.50 per share.

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2010 Private Placement

On August 9, 2010, the Company entered into a securities purchase agreement for the private placement (the "2010 Private Placement") of the Company's common stock and warrants to purchase its common stock, at a purchase price of $3.075 per unit, with each unit comprised of one share of common stock and a warrant to purchase one share of common stock. Each warrant, exercisable for 5 years from August 12, 2010, has an exercise price of $3.075 per share.

2011 Follow-on Public Offering

On September 13, 2011, the Company closed an underwritten public offering of shares of the Company's common stock at a price to the public of $4.00 per share. The shares sold in the offering included 10.0 million shares of common stock plus an additional 1.5 million shares of common stock pursuant to the exercise by the underwriters of the over-allotment option the Company granted to them. Total gross proceeds to the Company in the offering (including in connection with the sale of the shares of common stock pursuant to the exercise of the over-allotment option) totaled $46.0 million, before underwriting discounts and commissions. The offering resulted in net proceeds to the Company of approximately $42.8 million after deduction of underwriting discounts of 6% and other offering expenses paid by the Company.

Common Stock Issuance under At-The-Market ("ATM") Agreement

On April 30, 2012, the Company entered into an "At-the-Market" ("ATM") Sales Agreement with Cowen and Company, LLC ("Cowen"), under which the Company may, at its discretion, sell its common stock with a sales value of up to a maximum of $40 million through ATM sales on the NASDAQ Stock Market. Cowen acts as sole sales agent for any sales made under the ATM and receives a 3% commission on gross proceeds. The common stock is being sold at prevailing market prices at the time of the sale of common stock, and, as a result, prices may vary.

On July 3, 2013, the Company and Cowen amended and restated the Sales Agreement (the "Amended and Restated Sales Agreement") to increase the aggregate gross sales proceeds that may be raised to $100 million. Cumulatively through December 31, 2014, we sold 12,569,914 shares under the ATM offerings at a weighted-average selling price of $7.96 per share for net proceeds of approximately $97 million.

Sales in the ATM offerings are being made pursuant to the prospectus supplement dated April 30, 2012, as amended by Amendment No. 2 dated July 3, 2013, which supplements the Company's prospectus dated February 3, 2012, filed as part of the shelf registration statement that was declared effective by the Securities and Exchange Commission ("SEC") on February 3, 2012, and pursuant to the prospectus supplement dated August 21, 2014, which supplements the Company’s prospectus dated May 12, 2014, filed as part of the automatic shelf registration statement filed with the SEC on May 12, 2014. We did not sell any shares under ATM offerings during the nine months ended September 30, 2014. During the years ended December 31, 2014 and 2013, the Company sold approximately 5.0 million and 4.9 million shares, respectively, under ATM offerings at a weighted-average selling price of $9.29 and $8.09 per share, respectively, for proceeds of approximately $45 million and $38.8 million net of commissions, respectively. During the four month period ended December 31, 2012 and fiscal year ended August 31, 2012, the Company sold approximately 1.2 million shares and 1.5 million shares, respectively, at a weighted-average selling price of $5.10 and $5.34 per share, respectively, for net proceeds of approximately $6.0 million and $7.4 million, net of commissions, respectively. As of December 31, 2014, the Company did not have any remaining shares available under the ATM for future sales of the Company's common stock.

Common Stock Warrants

During the year ended December 31, 2014, the Company received approximately $1.8 million from the exercise of warrants in exchange for the issuance of 611,606 shares of the Company's common stock.

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The following table reflects the number of common stock warrants outstanding as of December 31, 2014.

	Number of Shares Exercisable	Exercise Price	Expiration Date
Issued in connection with Encode merger	233,309	$2.87	12/13/2015
TorreyPines warrants assumed in 2009 Merger	3,503	157.08	9/26/2015
Issued to placement agent in Aug. 2010	97,952	3.08	8/12/2015
Total Warrants Outstanding	334,764	$4.54 (1)	

(1) Weighted-average exercise price

The warrants issued by the Company in the August 2010 private placement and the December 2009 equity financing contain a conditional obligation that may require the Company to transfer assets to repurchase the warrants upon the occurrence of potential future events. Under ASC 480, a financial instrument that may require the issuer to settle the obligation by transferring assets is classified as a liability. Therefore, the Company has classified the warrants from both financings as liabilities and marks them to fair value at each period end. All warrants issued in connection with the December 2009 equity financing have been exercised or expired as of December 31, 2014.

A Black-Scholes option-pricing model was used to obtain the fair value of the warrants issued in the December 2009 and August 2010 equity financings. The following table presents the assumptions used at December 31, 2014 and 2013.

	August 2010 Private Placement Investors and Placement Agent		December 2009 Equity Financing Series A
	December 31,		December 31,
	2014	2013	2013
Fair value (in thousands)	$711	$6,933	$ 133
Black-Scholes inputs:			
Stock price	$10.28	$13.02	$ 13.02
Exercise price	$3.08	$3.08	$ 2.45
Risk free interest rate	0.12 %	0.33 %	0.13 %
Volatility	95.00%	95.00%	95.00 %
Expected term (years)	0.50	1.75	1.00
Dividend	-	-	-

For the years ended December 31, 2014 and 2013, the four months ended December 31, 2012 and the fiscal year ended August 31, 2011, the Company recorded losses of approximately $1.1 million, $10.7 million, $1.5 million, and $3.2 million, respectively, in its consolidated statements of operations and comprehensive loss from changes in the fair values of liability-classified warrants.

11. STOCK-BASED COMPENSATION

Stock Incentive Plans

In February 2010, the Company's Board of Directors approved, and in March 2010 Raptor's stockholders approved, the Raptor Pharmaceutical Corp. 2010 Stock Incentive Plan, as subsequently amended and approved by its stockholders in March 2011 ("Amended Plan"). On July 23, 2013, the Company, held its 2013 Annual Meeting of Stockholders (the "Annual Meeting"). At the Annual Meeting, Raptor's stockholders approved an amendment to the Amended Plan, which among other things, increased the authorized share reserve by 3,000,000 shares to an aggregate of 11,936,383 shares.

On November 25, 2014, as a key requirement of the Company's strategy of strengthening its leadership team and employee base, continuing the expansion of its commercial activities into new territories, and increasing the expansion of its product development programs, the Company's Board of Directors approved the Raptor Pharmaceutical Corp. 2014 Employment Commencement Stock Incentive Plan. The plan was approved pursuant to Rule 5635(c)(4) of the Nasdaq Global Select Market for equity grants to induce new employees to enter into employment with the Company. Up to 2,400,000 shares may be issued under this plan.

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As of December 31, 2014, there were 3,970,685 shares remaining available for issuance under both plans.

Stock options are granted to recognize the contributions made by its employees, independent contractors, consultants and directors, to provide those individuals with additional incentive to devote themselves to the Company's future success and to improve its ability to attract, retain and motivate individuals upon whom its growth and financial success depends. Employee stock options generally vest over four years with a six-month clift-vesting period. In general, all options are exercisable over a period not to exceed the contractual term of ten years from the date the stock options are granted at prices not less than the fair market value of the Company's common stock on the grant date. The Company has and may grant options with different vesting terms from time to time.

The following table presents components of stock-based compensation recorded in our consolidated statements of operations and comprehensive loss.

	Year Ended December 31,		For the Four Months Ended December 31,	For the Year Ended August 31,
(In thousands)	2014 [1]	2013	2012	2012
Cost of goods sold	$188	$-	$ -	$-
Research and development	2,191	1,550	453	926
General and administrative	9,554	5,480	1,786	3,633
Total Stock-Based Compensation Expense	$11,933	$7,030	$ 2,239	$4,559

(1) Stock-based compensation for the year ended December 31, 2014 does not include expense associated with the ESPP program of $113 thousand.

Stock-based compensation expense was based on the Black-Scholes option-pricing model assuming the following:

Period [1]	Risk-free interest rate	Expected life of stock option	Annual Volatility
Year ended December 31, 2014	0.0025% to 2.13%	6 years	67 to 68%
Four months ended December 31, 2013	0.68% to 0.7%	5 years	95%
Year ended August 31, 2012	0.68% to 1.2%	5 to 6 years	121 to 125%

(1) Dividend rate is 0% for all periods presented.

The compensation expense for stock-based compensation awards includes an estimate for forfeitures and is recognized over the requisite service period of the options, which is typically the period over which the options vest, using the straight-line method.

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A summary of the activity in the 2014 Employment Commencement Stock Incentive Plan, the 2010 Equity Incentive Plan, as amended, the 2006 Equity Compensation Plan, as amended, and the Company's other stock option plans, is as follows:

	For the Year Ended December 31, 2014		December 31, 2013	
	Option Shares	Weighted-average Exercise Price	Option Shares	Weighted-average Exercise Price
Beginning balance	8,217,674	$ 6.05	7,790,794	$ 5.79
Granted	3,356,946	12.03	1,187,500	9.21
Exercised	(1,643,464)	4.00	(651,386)	3.80
Canceled	(1,073,195)	14.22	(109,234)	34.89
Outstanding Balance at Year End	8,857,961	7.71	8,217,674	6.05

The number of options outstanding, vested and expected to vest as of December 31, 2014 was 8,390,147 and the weighted-average remaining contractual life was 6.8 years. The aggregate intrinsic value and the weighted-average intrinsic value of stock options outstanding, vested and expected to vest as of December 31, 2014 was $33.7 million and $7.57 per option, respectively. The number of options outstanding, vested and expected to vest as of December 31, 2013 was 8,109,622 and the weighted-average remaining contractual life was 7.6 years. The aggregate intrinsic value and the weighted-average intrinsic value of stock options outstanding, vested and expected to vest as of December 31, 2013 was $71.8 million and $8.85 per option, respectively.

As of December 31, 2014, the options outstanding under all of the Company's stock option plans consisted of the following:

	Options Outstanding			Options Vested and Exercisable		
Range of Exercise Price	Number of Options Outstanding	Weighted-average Remaining Contractual Life	Weighted-average Exercise Price	Number of Options Exercisable	Weighted-average Remaining Contractual Life	Weighted-average Exercise Price
$0 to $3.00	669,848	3.56	$ 2.61	669,848	3.56	$ 2.61
$3.01 to $5.00	1,357,975	5.09	3.80	1,249,480	4.86	3.72
$5.01 to $6.00	3,061,116	6.29	5.27	2,255,570	6.12	5.25
$6.01 to $8.00	738,872	8.37	7.11	273,306	7.95	6.90
$8.01 to $10.00	1,064,603	9.66	8.96	40,528	9.35	8.63
$10.01 to $14.00	568,696	8.84	12.42	121,481	7.50	12.76
$14.01 to $18.00	1,368,019	7.94	14.97	513,782	7.03	14.86
$18.01 to $965.00	28,832	1.57	100.58	28,832	1.57	100.58
Total	8,857,961	6.88	7.71	5,152,827	5.70	6.32

The aggregate intrinsic value of stock options outstanding as of December 31, 2014 was $34.5 million. The aggregate intrinsic value of stock options exercisable as of December 31, 2014 was $26.6 million.

At December 31, 2014, the total unrecognized compensation cost was approximately $21.5 million. The weighted-average period over which it is expected to be recognized is approximately 2.85 years.

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The following table presents details on the stock options granted and exercised.

(In thousands, except per share data)	Year Ended December 31, 2014	2013	For the Four Months Ended December 31, 2012	For the Year Ended August 31, 2012
Weighted-average fair value per share of options granted	$6.50	$5.33	$ 3.84	$ 4.62
Aggregate intrinsic value of options exercised	11,920	5,979	228	602

In the year ended December 31, 2014, the Company incurred $1.3 million of incremental stock compensation costs associated with modifications to two directors' and two employees' stock option grants. These modifications included the acceleration of unvested shares and an extended period to exercise vested options.

Employee Stock Purchase Plan

The ESPP allows a maximum of 1,000,000 shares of common stock to be purchased in aggregate for all employees. During 2014, the Company issued 21,280 shares under the ESPP. As of December 31, 2014, there were approximately 978,720 shares reserved for future issuance under the ESPP.

The assumptions used to estimate the per share fair value of stock purchase rights granted under the ESPP were as follows:

Period [1]	Risk-free interest rate	Expected life of stock option	Annual Volatility
Year ended December 31, 2014	0.01% to 0.16%	4 to 6 months	62% to 67%

(1) Dividend rate is 0%.

12. INCOME TAXES

The Company had losses before income taxes for domestic and foreign operations as follows:

(In thousands)	Year Ended December 31, 2014	2013	For the Four Months Ended December 31, 2012	For the Year Ended August 31, 2012
Domestic loss	$15,463	$33,966	$ 12,510	$26,642
Foreign loss	37,023	35,451	6,782	12,002
Loss before Income Taxes	$52,486	$69,417	$ 19,292	$38,644

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The provision for income taxes differs from the amount estimated by applying the statutory federal income tax rate to loss before taxes. The following is a reconciliation of the statutory federal and state rates to the effective rates, for the years ended December 31, 2014 and 2013, the four months ended December 31, 2012, and the fiscal year ended August 31, 2012.

Reconciliation of Statutory Tax Rate to Effective Tax Rate

	Year Ended December 31,		For the Four Months Ended December 31,	For the Year Ended August 31,
(In thousands)	2014	2013	2012	2012
Federal tax (benefit) at statutory rate	(34.00)%	(34.00)%	(34.00)%	(34.00)%
State tax (benefit) at statutory rate, net of federal tax benefit	(7.10)%	0.72 %	(3.72)%	(2.77)%
Change in valuation allowance	14.51 %	20.86 %	12.22 %	12.38 %
Research and development credits	(2.34)%	(14.92)%	- %	(2.68)%
Fair market value of warrants	- %	5.27 %	2.62 %	2.80 %
Intangible asset basis allocation	2.77 %	- %	8.69 %	7.66 %
Stock-based compensation - ISO	- %	1.08 %	3.93 %	3.96 %
Tax attributes not benefited	- %	6.07 %	- %	- %
Foreign losses not benefited	27.11 %	14.94 %	10.38 %	9.98 %
Other	(0.95)%	(0.02)%	(0.12)%	2.67 %
Effective Tax Rate	0 %	0 %	0 %	0 %

Components of our net deferred tax assets are presented in the following table.

Deferred Tax Assets

	December 31,	
(In thousands)	2014	2013
Net operating loss carryforwards	$22,480	$18,797
Capitalized start-up costs	11,057	11,256
Stock option expense	4,435	1,909
Research credits	20,951	19,281
Fixed assets and intangible assets	1,565	4,813
Accruals	1,434	1,224
Inventory	1,200	186
Other	124	65
Valuation allowance	(63,246)	(57,531)
Deferred Tax Assets, Net	$-	$-

As of December 31, 2014, the Company had net operating loss carryforwards for U.S. federal, U.S. state and foreign income tax purposes of approximately $51.5 million, $115.0 million and $2.9 million, respectively, which expire beginning after the year 2022, 2016 and 2021, respectively. As of December 31, 2014, the Company had federal and

state research and development credits of $20.0 million and $1.4 million, respectively. The federal credits expire beginning after the year 2026 and the state credits have no expiration.

As of December 31, 2014, the Company's net operating loss carryforwards for federal and state income tax purposes include approximately $7.5 million on a gross basis, respectively, of losses attributable to stock option tax expense deductions.

The valuation allowance increased approximately $5.7 million during the period ending December 31, 2014, primarily as a result of current year losses and tax credits.

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Utilization of the Company's net operating loss may be subject to substantial annual limitation due to the ownership change limitations provided by the Internal Revenue Code and similar state provisions. Such an annual limitation could result in the expiration of the net operating loss before utilization.

The Company has analyzed its tax positions in all of the federal, state and foreign jurisdictions where it is required to file income tax returns, as well as all open tax years in these jurisdictions.

As of December 31, 2014, the Company had no unrecognized tax benefits and has recorded no liability related to uncertain tax positions. The Company did not record a change in its unrecorded tax benefits during the year ended December 31, 2014, and expects no change in its unrecorded tax benefits in the next 12 months.

Due to net operating loss and research credit carryforwards, substantially all of the Company's tax years, from 2001 through 2014, remain open to U.S. federal and state tax examinations.

The Company is not aware of any pending income tax audits. Significant components of the Company's deferred tax assets for income tax purposes are net operating loss carryforwards, capitalized start-up costs, and stock-based compensation and research credits. Due to the Company's lack of earning history, any deferred assets recorded have been fully offset by a valuation reserve.

The Company's practice is to recognize interest and/or penalties related to income tax matters as a component of income tax expense. As of December 31, 2014, there were no accrued interest and penalties related to uncertain tax positions.

13. COMMITMENTS AND CONTINGENCIES

Contractual Obligations with UCSD Relating to the Acquisition of the DR Cysteamine (RP103) License

Pursuant to the license agreement with UCSD, the Company is obligated to pay milestone payments upon the occurrence of certain events, royalties on net sales from products developed pursuant to the license agreement and a percentage of sublicense fees or sublicense royalties, if any. The Company is obligated to fulfill predetermined milestones within a specified number of years from the effective date of the license agreement, depending on the indication. Cumulatively, the Company has expensed $2.2 million in milestone payments to UCSD based upon the initiation of clinical trials in cystinosis, Huntington's disease and NASH fand on regulatory filings in cystinosis. To the extent that the Company fails to perform any of its obligations under the license agreement, then UCSD may terminate the license or otherwise cause the license to become non-exclusive.

Leases

In April 2013, the Company executed a seven-year lease for its corporate office facilities in Novato, California. The Company took occupancy of such facilities at the end of June 2013. On June 10, 2013, the Company amended the lease to add space to accommodate its research laboratory and relocated to this space in July 2014. The Company records such rent on a straight-line basis.

In October 2014, the Company executed a three-year lease for its European sales, marketing and administrative headquarters in Utrecht, Netherlands. The Company records such rent on a straight-line basis.

Rent expense for the Company's current and previous facilities was approximately $1.3 million, $0.6 million, $0.1 million, and $0.2 million for the years ended December 31, 2014 and 2013, the four months ended December 31, 2012 and the fiscal year ended August 31, 2012, respectively. Leasehold improvements for our offices are amortized into expense over the lease term. There were $470 thousand of unamortized leasehold improvements at December 31, 2014. For the years ended December 31, 2014 and 2013, the four months ended December 31, 2012 and the fiscal year ended August 31, 2012, the Company recognized a negligible amount of leasehold amortization expense.

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The following table presents our future lease commitments at December 31, 2014:

(In thousands)	Future Lease Payments
2015	$ 1,553
2016	1,867
2017	1,901
2018	1,871
2019	1,929
2020 and thereafter	3,329
Total	$ 12,450

14. QUALIFYING THERAPEUTIC DISCOVERY PROJECT GRANT

In October 2010, the Company was awarded a tax grant under the U.S. Government's Qualifying Therapeutic Discovery Project for five of its research programs including its cystinosis, Huntington's disease and NASH clinical programs and its HepTide™ and WntTide™ preclinical cancer research programs. The Company was granted an aggregate of approximately $1.1 million for all five programs of which, as of August 31, 2011, it had received approximately $0.9 million. The Company recorded the $0.8 million of proceeds as a contra-research and development expense during the first two quarters of fiscal year 2011. During the fiscal year ended August 31, 2012, the Company received approximately $162 thousand pursuant to the government program funding guidelines and the remaining balance of approximately $36 was drawn but was returned to the government in March 2012 along with an additional $28 thousand as recapture tax because the Company had not incurred the amount originally estimated as qualified expenses for its WntTide™ program, which was the basis for the program funding. The Company recorded the contra-expense upon receipt of the grant proceeds.

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15. QUARTERLY RESULTS OF OPERATIONS (UNAUDITED)

The following table presents selected unaudited quarterly results of operations in conjunction with the consolidated financial statements and related notes contained elsewhere in this Annual Report on Form 10-K. These unaudited results were prepared on the same basis as the Company's audited consolidated financial statements. The Company's quarterly operating results have fluctuated in the past and may continue to do so in the future as a result of a number of factors, including, but not limited to, the timing and amounts of its revenues and the timing and nature of research and development activities.

	Quarterly Data 2014			
(In millions, except per share data, unaudited)	March 31, 2014	June 30, 2014	September 30, 2014	December 31, 2014
Net sales	$12.1	$16.3	$ 23.8	$ 17.3
Gross profit	10.8	15.3	19.8	14.0
Net loss	(14.9)	(12.7)	(6.0)	(18.9)
Net loss per share, basic and diluted	(0.24)	(0.20)	(0.10)	(0.29)

	Quarterly Data 2013			
(In millions, except per share data, unaudited)	March 31, 2013	June 30, 2013	September 30, 2013	December 31, 2013
Net sales	$-	$-	$ 6.7	$ 10.2
Gross profit	-	(0.4)	6.2	9.5
Net loss	(15.9)	(24.1)	(17.3)	(12.1)
Net loss per share, basic and diluted	(0.30)	(0.43)	(0.29)	(0.20)

(In millions, except per share data, unaudited)	Quarterly Data for the Four Months Ended December 31, 2012 November 30, 2012 [1]
Net loss	$(13.4)
Net loss per share, basic and diluted	(0.26)

	Quarterly Data 2012			
(In millions, except per share data, unaudited)	November 30, 2011	February 29, 2012	May 31, 2012	August 31, 2012
Net loss	$(11.4)	$ (14.0)	$(3.0)	$(10.2)
Net loss per share, basic and diluted	(0.25)	(0.29)	(0.06)	(0.21)

(1) The Company changed its fiscal year end to December; the four-month transition period included one quarterly report on Form 10-Q for the three months ended November 30, 2012.

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Schedule II: Valuation and Qualifying Accounts

Valuation Allowance for Deferred Tax Assets

(In millions)	Year Ended December 31, 2014	2013	Four Months Ended December 31, 2012	Fiscal Year Ended August 31, 2012
Balance at beginning of year	$ 58	$ 43	$ 41	$ 36
Additions to charged to expenses/other accounts	5	15	2	5
Net (deductions) recoveries	-	-	-	-
Balance at end of year	$ 63	$ 58	$ 43	$ 41