Raptor Pharmaceutical Corp
Form 424B5
August 21, 2014
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Filed Pursuant to Rule 424(b)(5)
Registration No. 333-195885

Calculation of Registration Fee

Title of Each Class of Securities to be Registered	Proposed Maximum Offering Price	Amount of Registration Fee(1)
Common Stock, par value $0.001 per share(2)	$46,193,473.43	$5,950

(1) Calculated pursuant to Rules 457(o) and 457(r) under the Securities Act of 1933, as amended (the Securities Act). The fee payable in connection with the offering of common stock pursuant to this prospectus supplement has been paid in accordance with Rule 456(b) and Rule 457(r) under the Securities Act.

(2) Includes associated rights to purchase shares of the registrant s Series A participating preferred stock par value $0.001 per share, or Purchase Rights, that are associated with all shares of the registrant s common stock, in accordance with that certain Rights Agreement, dated as of May 13, 2005, as amended, by and between the registrant and American Stock Transfer & Trust Company, LLC, as rights agent, or the Rights Agreement. The Purchase Rights are not exercisable until the occurrence of certain events specified in the Rights Agreement and, until the occurrence of certain events specified in the Rights Agreement, are evidenced by the stock certificates representing common stock and are transferrable only with the common stock. The value attributable to the Purchase Rights, if any, is reflected in the value of the common stock.

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Prospectus Supplement

(To prospectus dated May 12, 2014)

Shares of Common Stock, par value $0.001 per share

We have entered into a second amended and restated sales agreement with Cowen and Company, LLC, or Cowen, relating to shares of our common stock, offered by this prospectus supplement and the accompanying prospectus. In accordance with the terms of the second amended and restated sales agreement, we may offer and sell shares of our common stock having an aggregate offering price of up to $46,193,473.43. These shares are in addition to $53,806,526.57 of shares of common stock previously sold pursuant to the sales agreement, as amended and restated on July 3, 2013, and offered by the prospectus supplement dated April 30, 2012, as amended on July 3, 2013 (to prospectus dated February 3, 2012), under a shelf registration statement on Form S-3 (Registration No. 333-179215).

Our common stock is listed on The Nasdaq Global Market under the symbol RPTP. The last reported sale price of our common stock on The Nasdaq Global Market on August 19, 2014 was $11.44 per share.

Upon our delivery of a placement notice and subject to the terms and conditions of the second amended and restated sales agreement, Cowen may sell our common stock by methods deemed to be an at the market offering as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, or the Securities Act, including sales made directly on The Nasdaq Global Market, on any other existing trading market for our common stock or to or through a market maker. In addition, with our prior written approval, Cowen may also sell our common stock by any other method permitted by law, including in privately negotiated transactions. Cowen will act as sales agent using its commercially reasonable efforts consistent with its normal trading and sales practices and applicable state and federal laws, rules and regulations and the rules of The Nasdaq Stock Market LLC.

We will pay Cowen a commission, or allow a discount, for its services in acting as agent in the sale of our common stock equal to 3.0% of the gross sales price per share of all shares sold through it as agent under the second amended and restated sales agreement.

This investment involves a high degree of risk. See Risk Factors beginning on page S-7 of this prospectus supplement and in our periodic reports filed with the Securities and Exchange Commission and incorporated by reference herein for a discussion of the material risks you should consider before making an investment in our common stock.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

Cowen and Company

The date of this prospectus supplement is August 21, 2014

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, including the documents incorporated by reference herein, which describes the specific terms of this offering. The second part, the accompanying prospectus, including the documents incorporated by reference therein, provides more general information. Generally, when we refer to this prospectus supplement, we are referring to both parts of this document combined. Before you invest, you should carefully read this prospectus supplement, the accompanying prospectus, all information incorporated by reference herein and therein, as well as the additional information described under Where You Can Find More Information on page S-36 of this prospectus supplement. These documents contain information you should consider when making your investment decision. This prospectus supplement may add, update or change information contained in the accompanying prospectus. To the extent that any statement that we make in this prospectus supplement is inconsistent with statements made in the accompanying prospectus or any documents incorporated by reference therein, the statements made in this prospectus supplement will be deemed to modify or supersede those made in the accompanying prospectus and such documents incorporated by reference therein. You should not assume that the information appearing in this prospectus supplement, the accompanying prospectus, or information we previously filed with the Securities and Exchange Commission, or the SEC or the Commission, and incorporated by reference herein is accurate as of any date other than their respective dates, even though this prospectus supplement and any accompanying prospectus is delivered or shares of our common stock are sold on a later date. Our business, financial condition, results of operations and prospects may have changed since those dates.

You should rely only on the information contained or incorporated by reference in this prospectus supplement, the accompanying prospectus and in any free writing prospectuses we may provide to you in connection with this offering. We have not, and Cowen has not, authorized any other person to provide you with any information that is different. If anyone provides you with different or inconsistent information, you should not rely on it. We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the offering of our common stock in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement must inform themselves about, and observe any restrictions relating to, the offering of the common stock and the distribution of this prospectus supplement outside the United States. This prospectus supplement does not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

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FORWARD-LOOKING STATEMENTS

In this prospectus supplement and the accompanying prospectus, in other filings with 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, as amended, 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, continu 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. Such forward-looking statements, wherever they occur, are necessarily estimates reflecting the best judgment of our senior management on the date on which they were made, or if no date is stated, as of the date of the filing made with the SEC in which such statements were made. 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 as well as other factors not identified therein, and therefore we cannot guarantee future results, levels of activity, performance or achievements and you should not place undue reliance on any such forward-looking statements. We cannot give you any assurance that such forward-looking statements will prove to be accurate and such forward-looking events may not occur. 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 prospectus supplement to reflect later events or circumstances or to reflect the occurrence of unanticipated events or for any other reason.

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PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information concerning our business and this offering of shares of our common stock. It is not complete and does not contain all of the information that may be important to you and your investment decision. The following summary is qualified in its entirety by the more detailed information and consolidated financial statements and notes thereto included elsewhere or incorporated by reference into this prospectus supplement and the accompanying prospectus. You should carefully read this entire prospectus supplement and the accompanying prospectus, including the information incorporated by reference herein, and should consider, among other things, the matters set forth in Risk Factors before making an investment decision. References to the terms Raptor, and we, us, our or similar terms, refer to Raptor Pharmaceutical Corp. and its wholly-owned subsidiaries on a consolidated basis, unless we state or the context implies otherwise.

Overview

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

On April 30, 2013, our first product, PROCYSBI® (cysteamine bitartrate) delayed-release capsules, or PROCYSBI, received marketing approval from the U.S. Food and Drug Administration, or FDA, for the management of nephropathic cystinosis in adults and children six years and older. On September 6, 2013, our European equivalent, PROCYSBI® gastro-resistant hard capsules of cysteamine (as mercaptamine bitartrate), received a Community or EU marketing authorization from the European Commission, or EC, as an orphan medicinal product for the management of proven nephropathic cystinosis. 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 Free Trade Association, or EFTA). PROCYSBI received 7 years and 10 years of market exclusivity as an orphan drug in the U.S. and the EU, respectively. We commenced commercial sales of PROCYSBI in the U.S. in mid-June 2013 and in Germany in April 2014.

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.

RP103 Clinical Development

Huntington s Disease

Huntington s disease, or HD, is a rare, inherited neurodegenerative disorder. 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: chorea (jerky movements), neuropsychiatric symptoms, loss of executive functioning and dementia. HD is caused by an autosomal dominant mutation in a gene called huntingtin, which means any child of an affected person typically has a 50% chance of inheriting the disease. The huntingtin gene

encodes a protein that is also called huntingtin. Expansion of a CAG triplet repeat within the huntingtin gene results in a mutant form of the protein, which gradually damages

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cells in the brain. HD manifests as a triad of movement, cognitive and psychiatric symptoms which progress gradually in severity over 15-20 years, eventually causing severe physical and mental disability and potentially early 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 (with tetrabenazine, XENAZINE®, approved by FDA) and mood swings 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 potentially disease modifying treatment for HD. Centre Hospitalier Universitaire, or CHU, d Angers, France, is conducting the Phase 2/3 clinical trial of RP103. This 36-month randomized trial comprises an 18-month blinded, 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 the baseline of the Total Motor Score, or TMS, of the Unified Huntington s Disease Rating Scale, or UHDRS. TMS, a validated rating scale, is comprised of approximately 15 different tests that evaluate gross and small motor function in patients with HD. Chorea is a single measurement included in the TMS. The 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. Tetrabenazine is approved as a treatment for chorea associated with HD.

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. A mixed model analysis of all 96 patients enrolled in the trial showed slower progression of TMS in patients treated with RP103 versus those patients on placebo after 18 months treatment (4.51 vs. 6.68 respectively, p=0.19). While the results did not reach statistical significance, an overall positive trend was observed.

Patients were not randomized in the study based on concomitant medications 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 slower disease progression measured of TMS in the RP103 treatment arm versus those on placebo after 18 months treatment (2.84 vs.6.78 respectively (p= 0.03). The lower change of the TMS score for patients treated with RP103 represents a clinically significant slower rate of decline of more than 50% compared to those patients receiving placebo.

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 serious adverse events 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.

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

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Non-alcoholic Steatohepatitis

Non-alcoholic Steatohepatits, or NASH, is the hepatic component of metabolic syndrome and is associated with deposition of triglycerides in the hepatocytes in individuals who do not consume alcohol in amounts generally considered to be harmful to the liver. NASH 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. NASH is characterized by the histologic presence of inflammation (steatosis), cytological ballooning and pericellular fibrosis. Hepatic fibrosis resulting from NASH may progress to cirrhosis of the liver or liver failure, and in some instances may require a liver transplant or lead to hepatocellular carcinoma. There are no currently approved drug therapies to treat NASH.

NASH has historically been considered an adult disease, however more recent clinical evaluations have shown an alarming increased incidence of NASH among much younger populations. The number of suspected cases of NASH in children has risen dramatically, from below 4% in the mid 90s to nearly 11% between 2007 and 2010 Improvements in diet and increased exercise can have dramatic effects on reducing childhood NASH, and is always highly encouraged as an initial regimen to control the progression of this disease. However, absent substantial changes in lifestyle, NASH may eventually progress to liver failure in these adolescent patients.

RP103 as a treatment for NASH in children. In 2010, we conducted a Phase 2a clinical trial to examine RP103 as a treatment for NASH in children. Results of this trial showed that patients exhibited a marked decline in serum transaminase levels during the treatment period of 26 weeks. All patients had a mean 54% reduction in ALT (p=0.004), meeting the pre-defined primary endpoint of at least 50% ALT reduction from baseline. 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. In addition, patients saw statistically significant improvements in secondary endpoints including AST (41% average reduction, p=0.02), cytokeratin 18, a potential serum marker of disease activity in NASH, which decreased by an average of 45% (p=0.026), and adiponectin levels showed a positive increase by an average of 35% (p=0.023) during the treatment period. Reduced adiponectin levels are thought to be a marker of the pathogenesis and progression of NASH. Serum transaminases were measured following drug withdrawal and the reductions in ALT and AST persisted during the 6 month post-treatment phase.

In this Phase 2a clinical trial, the prototype of RP103 demonstrated a favorable safety profile, with mean gastrointestinal symptom scores of 1.1 (the maximum score of 14 indicates the most severe gastrointestinal symptoms) at baseline and 0.7 after six months of treatment. 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 NASH 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 NASH 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 as well as safety and tolerability. Top line clinical trial results for this study are anticipated in the first half of 2015.

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 U.S. is estimated to be 1 in 40,000 newborns.

RP103 as a treatment for mitochondrial disorders including Leigh Syndrome. We have submitted an investigational new drug application, or IND, to the FDA for the clinical development 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 trial is designed to evaluate the safety, tolerability and efficacy of RP103 in patients with genetically confirmed Leigh syndrome as well as patients with other mitochondrial disorders. The clinical plan includes an open label, 24 week, Phase 2/3 study in 32 patients (up to a maximum of 64 patients). Patients with Leigh syndrome are expected to comprise two-thirds of the enrolled population in the study. Initiation of the clinical trial is planned for the first half of 2014 at four clinical sites in the U.S. Based on an adaptive design statistical plan, we will conduct interim analyses after 12 patients and again after 24 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 in the first half of 2015.

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.

We own the intellectual property portfolio pertaining to Convivia, including method of use and formulation patents. In June 2010, we granted an exclusive license to commercialize Convivia in Taiwan to Uni Pharma Co., Ltd. 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 license Convivia.

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 Germany; 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 the second half of 2014; 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 our regulatory pathways and/or clinical trials of RP103 for the potential treatment of HD, NASH, Leigh syndrome and mitochondrial disorders; preparing for potential clinical studies of RP103 in new therapeutic indications; supporting our novel preclinical

programs; and identifying promising in-licensing candidates.

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.

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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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THE OFFERING

Common stock offered by us	Shares having an aggregate gross offering price of up to $46,193,473.43.
Manner of offering	At-the-market offering that may be made from time to time through our agent, Cowen and Company, LLC, or Cowen. See Plan of Distribution.
Use of proceeds	We expect to use the net proceeds from the offering to fund our commercial and pre-commercial efforts, our clinical and preclinical development programs and other general corporate purposes. See Use of Proceeds on page S-32 of this prospectus supplement.
Dividend policy	We intend to retain all future earnings, if any, to fund the development and growth of our business. We do not anticipate paying cash dividends on our common stock.
Risk factors	This investment involves a high degree of risk. See Risk Factors on page S-7 of this prospectus supplement and other information we include or incorporate by reference in this prospectus supplement and the accompanying prospectus.
Nasdaq Global Market symbol	RPTP

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RISK FACTORS

An investment in shares of our common stock involves a high degree of risk. Before you decide to invest in shares of our common stock, you should consider carefully all of the information in this prospectus supplement and the accompanying prospectus, including the risks and uncertainties described below, as well as other information included in or incorporated by reference into this prospectus supplement and the accompanying prospectus, particularly the specific risk factors discussed in the sections titled Risk Factors contained in our filings with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, before deciding whether to invest in shares of our common stock. Any of these risks could have a material adverse effect on our business, prospects, financial condition and results of operations. In any such case, the trading price of our common stock could decline and you could lose all or part of your investment.

Risks Related to Our Common Stock and this Offering

Management may invest or spend the proceeds of this offering in ways with which you may not agree and in ways that may not yield a return to our stockholders.

We will retain broad discretion over the use of proceeds from this offering. We expect to use the net proceeds from this offering to fund our commercial efforts, our clinical and preclinical development programs and other general corporate purposes. A number of variables will influence our actual use of the proceeds from this offering, and our actual uses of the proceeds of this offering may vary substantially from our currently planned uses. Management could choose to spend the net proceeds from this offering in ways in which stockholders may not deem desirable, or in ways that do not improve our operating results or result in a significant return or any return at all for our stockholders.

New investors in our common stock could experience immediate and substantial dilution.

The offering price of our common stock could be substantially higher than what the net tangible book value per share of our common stock is at the time of any offering. As a result, investors of our common stock in this offering could incur immediate and substantial dilution. After giving effect to the sale of our common stock in the maximum aggregate offering amount of $46.2 million at an assumed offering price of $11.44 per share, the last reported sale price of our common stock on The Nasdaq Global Market on August 19, 2014, and after deducting estimated offering commissions and expenses payable by us, our net tangible book value as of June 30, 2014 would have been approximately $56.9 million, or $0.85 per share of common stock. This represents an immediate increase in the net tangible book value of $0.65 per share to our existing stockholders and an immediate and substantial dilution in net tangible book value of $10.59 per share to new investors who purchase our common stock in the offering. See Dilution for a more detailed discussion of the dilution new investors will incur in this offering.

We may fail to meet publicly announced financial guidance or other expectations about our business, which would cause our stock to decline in value.

There are a number of reasons why we might fail to meet financial guidance or other expectations about our business, including, but not limited to, the following:

- unexpected difficulties in the commercialization of PROCYSBI in the U.S. or in the EU;

the effectiveness of our sales, marketing and distribution efforts and overall success of our commercialization efforts in the U.S. and in the EU;

lower than expected pricing and reimbursement levels, or no reimbursement at all, for PROCYSBI;

current and future competitive products that have or obtain greater acceptance in the market than PROCYSBI;

negative publicity about the results of our clinical trials, or those of others with similar or related products;

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if only a subset of or no affected patients respond to therapy with PROCYSBI or future products, if any;

the inability to sell a product at the price we expect; or

the inability to supply enough product to meet demand.

If we fail to meet our revenue and/or expense projections and/or other financial guidance for any reason, our stock price could decline.

Our stock price is volatile, which could result in substantial losses over short periods of time for our stockholders. 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. Our operating performance, both financial and in the development of approved products, affects and will continue to significantly affect the market price of our common stock. We face a number of risks including those described in this Risk Factors section, which may negatively impact the price of our common stock.

The market price of our common stock also may be adversely impacted by broad market and industry fluctuations including general economic and technology trends, regardless of our operating performance. The Nasdaq Global Market has, from time to time, experienced extreme price and trading volume fluctuations, and the market prices of securities of pharmaceutical, biotechnology and other life sciences companies in a comparable stage to us have historically been particularly volatile and trading volume in such securities has often been relatively small. Moreover, the stock markets in general have experienced substantial volatility that has often been unrelated to the operating performance of individual companies. The stock market also has periods during which industry segments, such as biotechnology, are in volatile swings of greater or lesser favor as investments. These swings may affect in particular 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 stage of company and our industry may experience a stronger degree of market sensitivity, will adversely affect the trading price of our common stock. In the past, following periods of volatility in the market resulting in substantial price declines 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 profitability and reputation.

A substantial number of shares of our common stock are eligible for future sale in the public market, and the issuance or sale of equity, convertible or exchangeable securities in the market, or the perception of such future sales or issuances, could lead to a decline in the trading price of our common stock.

Any additional issuance of equity, convertible or exchangeable securities, including for the purposes of raising capital to fund our operations, financing acquisitions and the expansion of our business, will have a dilutive effect on our existing stockholders. In addition, the perceived market risk associated with the possible issuance of a large number of shares of our common stock, including pursuant to the exercise of our currently outstanding stock options, or issuances of securities convertible or exchangeable into a large number of shares of our common stock could cause some of our stockholders to sell their common stock, thus causing the trading price of our common stock to decline. Subsequent sales of our common stock in the open market, exercises of our currently outstanding stock options and the subsequent sale of the shares acquired thereunder or the sale by us of shares of our common stock or securities convertible or exchangeable into our common stock for capital raising purposes could also have an adverse effect on

the trading price of our common stock. If our common stock price declines, it will be more difficult for us to raise additional capital or we may be unable to raise additional capital at all.

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 a conversion rate of 57.14 shares of common stock per $1,000 principal amount of convertible senior notes, which is equivalent to an initial

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conversion price of $17.50, and is 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.

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 existing and future 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. As a result, the success of an investment in our common stock will depend upon any future appreciation in the value of our common stock. There is no guarantee that our common stock will appreciate in value or even maintain its current price. Investors seeking dividend income should not invest in our common stock.

We can issue shares of preferred stock that may adversely affect the rights of a stockholder of our common stock.

Our certificate of incorporation authorizes us to issue up to 15.0 million shares of preferred stock with designations, rights and preferences determined from time-to-time by our board of directors. Accordingly, our board of directors is empowered, without stockholder approval, to issue preferred stock with dividend, liquidation, conversion, voting or other rights superior to those of stockholders of our common stock.

Anti-takeover provisions under Delaware law, in our stockholder rights plan and in our certificate of incorporation and bylaws 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.

We are incorporated in Delaware. Certain anti-takeover provisions of Delaware law as currently in effect may make a change in control of our Company more difficult, even if a change in control may be beneficial to the stockholders. Our board of directors has the authority to issue up to 15.0 million shares of preferred stock, none of which are issued or outstanding. The rights of holders of our common stock are subject to the rights of the holders of any preferred stock that may be issued. The issuance of preferred stock could make it more difficult for a third-party to acquire a majority of our outstanding voting stock. Our certificate of incorporation contains provisions that may enable our management to resist an unwelcome takeover attempt by a third party, including: a prohibition on actions by written consent of our stockholders; the fact that stockholder meetings must be called by our board of directors; and provisions requiring stockholders to provide advance notice of proposals. Delaware law also prohibits corporations from engaging in a business combination with any holders of 15% or more of their capital stock until the holder has held the stock for three years unless, among other possibilities, the board of directors approves the transaction. Our board of directors may use these provisions to prevent changes in the management and control of our Company. Also, under applicable Delaware law, our board of directors may adopt additional anti-takeover measures in the future.

We are a 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 and less desirable to the potential acquirer. The stockholder rights plan and our certificate of incorporation and bylaws, as amended, contain provisions that may discourage, delay or prevent a merger, acquisition or other change in control that stockholders may consider favorable,

including transactions in which stockholders might otherwise receive a premium for their shares. These provisions could limit the price that investors might be willing to pay in the future for shares of our common stock.

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Risks Associated with Commercialization and Product Development

We 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 operating results are substantially dependent on the commercial success of PROCYSBI, for which we commenced marketing in the U.S. in June 2013 and in Germany in April 2014. In the U.S., 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 EC, which 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 Free Trade Association, or EFTA), for the treatment of proven nephropathic cystinosis; however, we only recently commenced our commercial launch of PROCYSBI in Germany and have not yet launched in any other country in the EU. We believe that the trading price of our common stock will be substantially affected by our results of operations and, in particular, net product sales of PROCYSBI. We do not have prior experience in commercializing therapeutics. If PROCYSBI sales do not meet expectations, our stock price may not increase or could significantly decrease. The successful commercialization of PROCYSBI will depend on several factors, including:

- the success of our ongoing commercial launch of PROCYSBI in Germany;
- the negotiation and agreement on an acceptable prices in EU countries and other select territories, and reimbursement at the country-specific price;
- the successful commercial launch of PROCYSBI in the EU and other select territories;
- acceptance of PROCYSBI by physicians, parents, patients and cystinosis research/advocacy organizations including the conversion from the existing standard of care to PROCYSBI;
- coverage and reimbursement for PROCYSBI from commercial health plans and government health programs, which we refer to collectively as third-party payors;
- compliance with regulatory requirements including fulfilling any FDA and EC required post-approval commitments;
- provision of affordable out-of-pocket cost to patients and/or other programs to ensure patient access to PROCYSBI in the U.S.;
- approval by regulatory agencies in other countries of appropriate product labeling for PROCYSBI;

agreements with wholesalers, distributors and pharmacies on commercially reasonable terms;

manufacture and supply of adequate quantities of PROCYSBI to meet commercial demand; and

development and maintenance of intellectual property protection for PROCYSBI.

If we fail to grow sales of PROCYSBI in the U.S. or Germany or successfully commercialize PROCYSBI in the other countries in the EU within a reasonable time period, we may never become profitable and may be unable to sustain our business, and our business, financial condition and results of operations will be 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. 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:

availability and relative efficacy, safety and ease of administration of alternative treatments;

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the price of our product, both in absolute terms and relative to alternative treatments;

timing of market introduction of our product as well as competitive drugs;

ease of use, efficacy, safety and prevalence and severity of any side effects of PROCYSBI;

identification of currently diagnosed and undiagnosed patients and continued growth of the cystinosis market;

acceptance by patients, patient families and primary care and other specialists including conversion from the existing standard of care;

continued patient adherence to therapy;

the effect of current and future healthcare laws;

availability of coverage and adequate reimbursement and pricing from third-party payors; and

breadth of product labeling or product insert requirements of the FDA, EC or other regulatory authorities.

If PROCYSBI does not achieve and maintain significant market acceptance among physicians, patients, patient families, third-party payors or the healthcare community, our ability to generate revenues from PROCYSBI will be materially and adversely affected.

The amount of our product sales of PROCYSBI in the EU is dependent upon the pricing and reimbursement guidelines adopted in each of the various countries in the EU, which levels may be below our current expectations.

While we are developing estimates of anticipated pricing in EU countries other than Germany, one or more EU countries may not support our anticipated pricing and reimbursement for PROCYSBI, particularly in light of the budget crises faced by a number of countries in the EU, which would negatively affect anticipated revenue from PROCYSBI. The pricing and reimbursement process in the EU 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 EU will delay our ability to market PROCYSBI in the EU and derive product sales in that region.

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

We must 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. In the U.S., we are permitted to market RP103 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 EU as an orphan medicinal product for the treatment of proven nephropathic cystinosis. We do not have approval of RP103 in any other market or for any other disease indication. A new drug application, or NDA, submitted to the FDA or marketing authorization application, or MAA, submitted to the EMA must be supported by extensive clinical and preclinical data, as well as extensive information regarding chemistry, manufacturing and controls, to 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:

- the results of clinical trials may not meet the level of statistical or clinical significance required by regulatory authorities for approval;

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regulatory authorities may disagree with the number, design, size, conduct or implementation of our clinical trials; may not find the data from preclinical studies and clinical trials sufficient to demonstrate that a product candidate has adequate clinical and other benefits or an adequate safety profile; or 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, limitations on approved labeling or distribution and use restrictions;

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 impose limitations on approved labeling, thus introducing reimbursement complications which may limit access for intended uses or limit the commercial profile of the drug;

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;

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; or

regulatory authorities may change approval policies or adopt new regulations.

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

We do not have internal manufacturing capabilities. During 2014 and throughout most of 2015, we expect to continue to rely on a single supplier for the active pharmaceutical ingredient and a single third-party manufacturer for the conversion to finished drug product. If we are unable to obtain an adequate supply of our drugs, our reputation will be harmed, our revenue will be delayed or diminished and our financial results will be adversely affected.

Using external contract manufacturing organizations, or CMOs, we currently manufacture commercial and clinical quantities of PROCYSBI and RP103 for the indications under development. We rely on single manufacturing sources for our cysteamine active pharmaceutical ingredient, or API, and finished products. Our ability to obtain sufficient quantities of PROCYSBI and RP103 is constrained by limited supplies of raw materials and capacity and output of these manufacturers. Furthermore, any reduction or interruption in our supply of API from the single source supplier

and of finished goods from our CMO, and efforts to identify and qualify alternative sources of API supply, could result in significant additional operating costs, interruptions in product supply and delays in sales of PROCYSBI and in developing RP103 for HD, NAFLD and Leigh s syndrome. In addition, supply arrangements from alternative sources 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 production costs and yields, quality control, including stability of the product or product candidates 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. In addition, due to our small patient population, the manufacture of our drug may be given lower prioritization on the production line if manufacturing is decided by scale.

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We depend on our third-party supplier and manufacturers for compliance with the FDA s current good manufacturing practices, or cGMP, requirements and other FDA requirements, Drug Enforcement Administration s regulations and other rules and regulations prescribed by applicable non-U.S. regulatory authorities. We do not control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with cGMP requirements. If our CMOs cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. In addition, we have no direct control over the ability of our CMOs to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the continued manufacture of our product or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to market PROCYSBI and to develop, obtain regulatory approval for or market our product candidates, if approved. If we or our third-party suppliers and manufacturers fail to comply with applicable regulatory requirements, a regulatory agency may issue warning letters or untitled letters; seek an injunction or 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.

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, financial condition and results of operations would be adversely affected.

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. Additionally, PROCYSBI and our future product candidates, if approved, may be subject to labeling and other restrictions or potential market withdrawal, and we may be subject to penalties and litigation if we fail to comply with regulatory requirements or experience problems with our products.

Our manufacturing processes, labeling, packaging, distribution, storage, adverse event reporting, dispensation, distribution, advertising, promotion and recordkeeping are subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, ongoing maintenance of product registration, as well as continued compliance with cGMPs, good clinical practices, or GCPs, good distribution practices, or GDPs, and good laboratory practices, or GLPs. If we do not comply with applicable regulations and requirements, the range of possible sanctions includes adverse publicity, product recalls or seizures, fines, total or partial suspensions of production and/or distribution, suspension of marketing applications, withdrawal of a product s approval and enforcement actions, including injunctions and civil or criminal prosecution. In addition, if we or a regulatory agency discover previously unknown problems with PROCYSBI, such as adverse events of unanticipated severity or frequency, or identify data that suggest that PROCYSBI may present a risk to safety, the regulatory authorities could withdraw our product approval, suspend production or place other marketing restrictions on our products. If regulatory sanctions are applied or if regulatory approval is withdrawn, our growth prospects and our operating results will be adversely affected.

Moreover, any regulatory approvals that we obtain will be subject to limitations on the approved indicated uses for which the product may be marketed or the conditions of approval, or contain requirements for potentially costly post-market testing and surveillance to monitor the safety and efficacy of the product. The FDA and EC strictly regulate the promotional claims that may be made about prescription products and our product labeling, advertising and promotion is 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. The FDA, the Competent Authorities of the Member States of the Economic European Area, or EEA, and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and 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.

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In addition, engaging in improper promotion of our products for off-label uses in the U.S. can subject us to false claims litigation under federal and state statutes, which can lead to consent decrees, civil money penalties, restitution, criminal fines and imprisonment, and exclusion from participating in Medicare, Medicaid and other federal and state health care programs. These false claims statutes in the U.S. 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. If the government prevails in the lawsuit, the individual will share in any fines or settlement funds. Growth in false claims litigation has increased the risk that a pharmaceutical company will have to defend a false claim action, pay 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. In addition, various states have enacted false claim laws analogous to the federal False Claims Act, some of which may apply to claims submitted to any third party payor and not only a governmental payor program.

In the EEA, the advertising and promotion of pharmaceuticals is strictly regulated, and the direct-to-consumer promotion of prescription pharmaceuticals is not permitted. The Member States of the EEA have also adopted laws against misleading and unfair advertising. In addition, some Member States require the notification and/or prior authorization of promotional or advertising materials directed at health care professionals. Failure to comply with these regulations can lead to the imposition of administrative fines and criminal penalties, civil litigation leading to injunctive relief to stop the advertising, corrective statements, or damages.

If serious adverse side effects become associated with PROCYSBI, our business will be harmed.

The prescribing information for PROCYSBI includes several warnings relating to observed adverse reactions of cysteamine bitartrate usage. These adverse reactions were not observed in our clinical trials supporting PROCYSBI s NDA and MAA, but were required on our label due to our submission of a 505(b)(2) application in the U.S. and a hybrid application in the EU. The FDA may require products approved under Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act to bear the same or similar warning statements as the reference product. 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, or we may choose to withdraw PROCYSBI from the market. If this were to occur, we may be unable to 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, financial condition and results of operations.

See also the risk factor titled We may be subject to product liability claims.

Pressure on drug product third-party payor coverage, reimbursement and pricing may impair our ability to be reimbursed for PROCYSBI and our other future product candidates at prices or on terms sufficient to provide a viable financial outcome.

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 U.S. as well as the EEA countries and other key international markets. The continuing efforts of governmental and 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 medical products and services, particularly for

new and innovative products and therapies, may result in downward pressure on product pricing, reimbursement and utilization, which may adversely affect our 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, drug coverage and reimbursement policies and pricing in general. Moreover, private health insurers and other third-

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party payors in the U.S. often follow the coverage and reimbursement policies of government payors, including the Medicare or Medicaid programs. In the U.S., third-party payors are shifting their cost containment measures to specialty products and high-cost drugs and PROCYSBI may be a target of such measures.

Beginning April 1, 2013, Medicare payments for all items and services under Part A and B, including drugs and biologicals, and most payments to plans under Medicare Part D were reduced by 2% under the automatic spending reductions, or sequestration, required by the Budget Control Act of 2011, or BCA, as amended by the American Taxpayer Relief Act, or ATRA. The BCA required sequestration for most federal programs, excluding Medicaid, Social Security and certain other programs, because Congress failed to enact legislation by January 15, 2012 to reduce federal deficits by $1.2 trillion over 10 years. As long as BCA cuts remain in effect, they could adversely impact payment for PROCYSBI. In addition, other recent legislative changes that increase manufacturer liability for rebates and other payments under the 340B drug pricing program, the Medicaid Drug Rebate Program and the Medicare Part D prescription drug benefit also could impact our revenues. See also the risk factor titled Enacted and future legislation 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.

Further, payors also are increasingly considering new metrics as the basis for reimbursement rates, such as average sales price, or ASP, average manufacturer price, or AMP, or actual acquisition cost, or AAC. Although the intent of the changes to reimbursement methodologies generally is 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. Although to date PROCYSBI has been reimbursed in the U.S. and Germany, we do not know whether third-party payors will reimburse PROCYSBI in the other EEA countries or continue to reimburse PROCYSBI in the U.S. and whether third-party payors will reimburse RP103 and our future products for future commercial indications until we enter into payor negotiations. If coverage and reimbursement are not available or available only to limited levels, we may not be able to generate sufficient revenue to meet our operating costs or to achieve our revenue, cash flow breakeven or profitability goals in the timeframe that we expect, or at all.

Enacted and future legislation 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 U.S., there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that restrict or regulate post-approval activities, which may affect our ability to profitably sell PROCYSBI or any other product candidate for which we obtain marketing approval.

The Medicare Prescription Drug Improvement and Modernization Act of 2003, or MMA, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for outpatient drug purchases by those covered by Medicare under a new Part D and introduced a new reimbursement methodology based on average sales prices for Medicare Part B physician-administered drugs. In addition, this legislation authorized Medicare Part D prescription drug plans to use formularies whereby they can limit the number of drugs that will be covered in any therapeutic class. As a result of this legislation and the expansion of federal coverage of drug products, there is additional pressure to contain and reduce costs. While the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates, and any reduction in reimbursement that results from the MMA may result in a similar reduction in payments from private payors. These cost reduction initiatives and other provisions of the MMA could decrease the coverage and reimbursement that we receive for any approved products, and could seriously harm our business. Manufacturers contributions to this area, including donut hole coverage (as described below) or potential excise taxes, are increasing and are subject to additional changes in the future.

In 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (together, the Health Care Reform Law), a sweeping law intended 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

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health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. The Health Care Reform Law, among other things, revised the definition of AMP for reporting purposes, which could increase the amount of Medicaid drug rebates to states and extended the rebate program to beneficiaries enrolled in Medicaid managed care organizations. The Health Care Reform Law also 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 U.S. The Health Care Reform Law also expanded the 340B drug discount program (excluding orphan drugs), including the creation of new penalties for non-compliance and included a 50% discount on brand name drugs for Medicare Part D participants in the coverage gap, or donut hole. The Health Care Reform Law includes a provision to increase the Medicaid rebate for line extensions or reformulated drugs, which depending on how this provision is implemented could substantially increase our Medicaid rebate rate (in effect limiting reimbursement for these patients). These and other new provisions are likely to continue the pressure on pharmaceutical pricing, may require us to modify our business practices with healthcare practitioners, and may also increase our regulatory burdens and operating costs. See the risk factor titled Failure to comply with healthcare regulations may subject us to substantial penalties.

Legislative and regulatory proposals also have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. In addition, 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. Delays in feedback from the FDA may affect our ability to quickly update or adjust our label 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 specifically the commercialization of PROCYSBI.

Failure to comply with healthcare regulations may subject us to substantial penalties.

Although we do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payors, 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. The laws that may affect our ability to operate as a commercial organization 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;

- 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;

- federal criminal laws that prohibit executing a scheme to defraud any federal healthcare benefit program or making false statements relating to healthcare matters;

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 the Centers for Medicare & Medicaid Services, or 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 applicable manufacturers and group purchasing organizations to report annually to CMS ownership

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and investment interests held by physicians (as defined above) and their immediate family members and payments or other transfers of value to such physician owners and their immediate family members. Manufacturers were required to begin data collection on August 1, 2013 and to report aggregate data to the government by March 31, 2014 with more detailed reports due by June 30, 2014;

in the EU, in various Member States, including France, the UK, the Netherlands, Italy, or Spain, the legislator or self-regulatory industry bodies have adopted rules requiring the notification and/or publication of certain transfers of value from pharmaceutical companies to health care 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 health care professionals; and

analogous state and foreign law equivalents of each of the above federal laws, including, but not limited to anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers.

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, the Health Care Reform Law further strengthened these laws by amending the intent requirement of the federal anti-kickback and criminal health care fraud statutes. A person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it. In addition, the Health Care Reform Law provides that the government may assert that a claim including items or services resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim for purposes of the false claims statutes. 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.

Moreover, there has been a recent trend of increased federal and state regulation of payments made to physicians for marketing. Certain states mandate implementation of compliance programs and/or the tracking and reporting of gifts, compensation, and other remuneration to physicians. The shifting compliance environment and the need to build and maintain robust and expandable systems to comply with multiple jurisdictions with different compliance and/or reporting requirements increase the possibility that a healthcare company may violate one or more of the requirements.

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 health care providers, some of whom recommend, purchase and/or prescribe our products, could be subject to challenge under one or more of such laws. While these activities are structured to comply with all applicable laws, if our operations are found to be in violation of 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 adversely impact our financial results. 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 U.S., we could be subject to additional reimbursement requirements, penalties, sanctions and fines which could have a material adverse effect on our business, financial condition, results of operations and future business prospects.

As we expand our development and commercialization activities outside of the U.S., we will be subject to an increased risk of inadvertently conducting activities in a manner that violates the U.S. Foreign Corrupt Practices Act, or FCPA, and similar laws. If that occurs, we may be subject to civil or criminal penalties which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

We are subject to 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,

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political party, or political candidate in an attempt to obtain or retain business or to otherwise influence a person working in an official capacity. We are also subject to the UK Bribery Act, which prohibits both domestic and international bribery, as well as bribery across both public and private sectors.

In the course of establishing and expanding our commercial operations and seeking regulatory approvals outside of the U.S., 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, 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 substantial fines and penalties and could materially harm our business. Furthermore, any finding of a violation under one country s laws may increase the likelihood that we will be prosecuted and be found to have violated another country s laws. If our business practices outside the U.S. are found to be in violation of the FCPA, UK Bribery Act or other similar law, we may be subject to significant civil and criminal penalties which could have a material adverse effect on our business, financial condition and results of operations.

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

We participate in the Medicaid Drug Rebate Program and other Federal and state government pricing programs in the U.S., and we may participate in additional government pricing programs in the future. These programs generally require us to pay rebates or 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. 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, and could have a material adverse effect on our results of operations.

Pricing and rebate calculations vary among products and programs. The calculations are complex and are often subject to interpretation by governmental or regulatory agencies and the courts.

In addition, the Office of Inspector General has recently increased its focus on the methodologies used by manufacturers to calculate 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 overcharging 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.

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

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 HD, respectively. A key component of the successful commercialization of a drug product for these indications includes identification of 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 and identifying patients and targeting the prescriber base are key to achieving significant market penetration. In addition, the per-patient prices at which we sell PROCYSBI (currently estimated at an average of $265,000 per year after rebates, discounts, distribution fees and adjusted for patient compliance in the U.S.) 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 achieve meaningful gross margins. There can be no assurance that we will be successful in achieving a sufficient degree of market penetration and/or obtaining or maintaining high per-patient prices for PROCYSBI and RP103 for diseases with small patient populations. Further, even if we obtain significant market share for PROCYSBI and RP103, if approved, because the potential target populations are very small, we may never achieve profitability despite obtaining such significant market share. Additionally, patients who discontinue therapy or do not fill prescriptions are not easily replaced by new patients, given the limited patient population.

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

As part of our business strategy, we intend to develop RP103 for additional indications and other drugs 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 U.S., or a patient population greater than 200,000 in the U.S. where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the U.S. In the U.S., 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, with an additional six months if for a pediatric indication. Orphan drug exclusive marketing rights may be lost if the FDA later determines that the request for designation was materially defective, a subsequent product is deemed clinically superior, or if the manufacturer is unable to deliver sufficient quantity of the drug. We also may not successfully obtain orphan drug designations for our product candidates, or be able to obtain requisite approvals for the stated condition of our orphan drug designations.

In the EU, the European Medicine Agency s, or 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 EU 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). 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 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. An 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.

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 products that are eligible for orphan drug designation. For eligible drugs, we plan to rely on the orphan exclusivity period to maintain a competitive position. However, if we do not

obtain orphan drug exclusivity for RP103 for the potential treatment of HD or other potential indications, or our future relevant drug products do not have strong patent protection, our competitors may then sell the same drug to treat the same condition and our revenues will be reduced. Also, without strong patent protection, competitors may sell a generic version upon the expiration of orphan exclusivity, if our patent position is not upheld.

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Even though we have been granted orphan drug designation in the U.S. and 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. The FDA can discontinue orphan drug exclusivity after it has been granted if the orphan drug cannot be manufactured in sufficient quantities to meet demand. 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 immediate-release cysteamine bitartrate s lower cost and our 505(b)(2) filing status.

A breakthrough designation or fast track designation for our drug product candidates, if obtained, may not actually lead to a faster review process.

Under the Prescription Drug User Fee Act, the FDA has a goal of responding to NDAs within 10 months of submission the filing date for standard review, but this timeframe is also often extended. In the future, we may seek approval of our drug candidates under programs designed to accelerate the FDA s review and approval of NDAs. 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 some cases, a product may be approved 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. Approvals of this kind typically include requirements for appropriate post-approval Phase 4 clinical trials to validate the surrogate endpoint or otherwise confirm the effect of the clinical endpoint. In addition, the Food and Drug Administration Safety and Innovation Act, or FDASIA, which was enacted and signed into law in 2012, 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, 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. In the future, we may request breakthrough designation or fast track designation from the FDA for our other drug product candidates, but we cannot assure 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 FDA approval of 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 requesting additional clinical studies (although potentially a post-marketing requirement), during its review. Any request for additional information or clinical data could delay the FDA s timely review of our NDA.

We may not be successful in integrating our European operations with our U.S. operations.

In connection with the EU commercial launch of PROCYSBI, 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 include the

following:

- the potential strain on our financial and managerial controls and reporting systems and procedures;

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potential miscommunication between U.S. personnel and European personnel due to cultural and language differences;

the small size of our company and our intention to grow at a consistent but measured pace;

ability to operate within diverse individual country regulatory and statutory laws; and

the costs of maintaining EU presence, in-country legal entities and related tax structures.

If we fail to obtain and maintain approval from regulatory authorities in international markets for PROCYSBI, RP103 and any future product candidates for which we have rights in international markets, our market opportunities will be limited and our business will be adversely impacted.

Sales of our products outside of the U.S. are 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 U.S., including additional preclinical studies or clinical trials or manufacturing and control requirements. In many countries outside the U.S., 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 and 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.

Clinical drug development involves a lengthy and expensive process with an uncertain outcome and results of earlier studies and trials may not be predictive of future trial results. If we fail to demonstrate safety or efficacy in our preclinical studies or clinical trials or keep to the terms of a product development program, our future business prospects for these drug product candidates will be materially adversely affected.

The success of our development and commercialization efforts will be greatly dependent upon our ability to demonstrate safety and efficacy in preclinical studies and clinical trials. Preclinical studies involve testing in appropriate multiple non-human disease models to demonstrate efficacy and safety. Regulatory agencies evaluate these data carefully before they will authorize clinical testing in humans. If certain preclinical data reveal potential safety issues or 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. 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. 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.

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. 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 would 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

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or clinical trials will delay the filing of relevant marketing applications with the regulatory agencies and, ultimately, our ability to commercialize our drug product candidates and generate product revenues.

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 availability of alternative therapies and drugs, the proximity of patients to clinical sites, the eligibility criteria for the study, competing clinical trials and clinicians and patients perceptions as to the potential advantages of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating. Delays in planned patient enrollment may result in increased costs and delays. We do not know whether our IND 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 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;
- delays or failures in reaching agreement on acceptable clinical trial agreement terms or clinical trial protocols with prospective sites; and
- delays or failures in obtaining Institutional Review Board, or IRB, approval to conduct a clinical trial at a prospective site.

The completion of our clinical trials could also be substantially delayed or prevented by several factors, including:

- slower than expected rates of patient recruitment and enrollment;
- failure of patients to complete the clinical trial;
- unforeseen safety issues;

lack of efficacy during clinical trials;

inability or unwillingness of patients or medical investigators to follow our clinical trial protocols;

inability to monitor patients adequately during or after treatment; and

regulatory action by the FDA for failure to comply with regulatory requirements.

In addition, many of our clinical trials involve small patient populations. Because of the small sample size, the results of these early clinical trials may not be indicative of future results. 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 future business prospects, financial condition and results of operations.

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 or allegedly harm people and we may be subject to costly and damaging product liability claims. Many of the patients who participate in our current clinical trials and U.S. and EU cystinosis patients who may purchase PROCYSBI commercially are already critically ill or suffering from chronic debilitating diseases. The waivers we obtain from patients participating 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 future claims. If a successful product liability claim is brought against us and the amount of liability exceeds our insurance coverage, we may incur substantial charges that would adversely affect our business, financial condition and results of operations.

We rely on third parties for the distribution and pharmaceutical services of PROCYSBI in the U.S. and the EU.

We rely on a third-party logistics provider and specialty pharmacy to distribute PROCYSBI to patients in the U.S. and to pharmacies in Germany and to collect from insurance companies and government agencies in the U.S. and from pharmacies in the EU. Our ability to collect from the U.S. 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 harm our reputation 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;

clinical research organizations;

distribution and supply (logistics) service organizations;

contract testing organizations;

consultants or consulting organizations with specialized knowledge based expertise;

intellectual property legal firms; and

multiple other service organizations.

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 contract research organizations and/or co-operative groups, to assist us in overseeing and monitoring clinical trials as well as to process the clinical results. If third parties fail to perform or to meet the applicable standards, this will result in delays in or failures to complete trials. A failure by us or such third parties to observe the terms of a product development program

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for any particular product candidate or to complete the clinical trials for a product candidate in the anticipated time frame could have significant negative repercussions on our business and financial condition.

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

- 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 pivotal to establishing products using our technologies 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 research partners. 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 successfully develop PROCYSBI, RP103 or our other drug product candidates.

We will continue to incur increased costs as a result of corporate governance and financial reporting laws and regulations and our management will continue to be required to devote substantial time to comply with such laws and regulations.

We face burdens relating to increased corporate governance and financial reporting standards. Legislation or regulations, such as the Physician Payment Sunshine Act, the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, and the Dodd-Frank Wall Street Reform and Consumer Protection Act, as well as other rules implemented by the FDA, the SEC and The Nasdaq Global Market, follow stricter corporate governance and financial reporting standards and have led to an increase in the costs of compliance, including substantial increases in consulting, auditing and legal fees. Our management and other personnel will need to devote a substantial amount of time to these requirements. New rules could make it more difficult or more costly for us to obtain certain types of insurance, including directors and officers liability insurance, and we may be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. The impact of these events could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, on our board committees or as executive officers. Failure to comply with these new laws and regulations may impact our financial condition and could materially harm our business.

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In addition, 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. Our compliance with Section 404 requires that we incur substantial accounting and related expense and expend significant management efforts. Moreover, if we are not able to comply with the requirements of Section 404, or we or our independent registered public accounting firm identifies deficiencies in our internal control over financial reporting that are deemed to be material weaknesses, the market price of our stock could decline and we could be subject to sanctions or investigations by The Nasdaq Global Market, the SEC or other regulatory authorities.

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

Continued commercial sales of PROCYSBI in the U.S., the EU commercial launch of PROCYSBI, expansion of our commercial operations into other markets, the continuation of our clinical-stage programs and our current plans to in-license and acquire additional clinical-stage product candidates will require us to retain existing and add required new qualified and experienced personnel in all functional areas over the next several years. Also, if our preclinical pipeline diversifies through internal discoveries, or the acquisition or in-licensing of new molecules, we will need to hire additional scientists to supplement our existing scientific expertise over the next several years.

Our staff, financial resources, systems, procedures or controls may be inadequate to support our expanding operations and our management may be unable to take advantage of future market opportunities or manage successfully our relationships with third parties if we are unable to adequately manage our anticipated growth and the integration of new personnel.

Our loan agreement with HC Royalty contains 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 could have an adverse impact on our business and financial condition.

In December 2012, we entered into a loan agreement with HC Royalty as lender, under which we agreed to borrow $50.0 million in two $25.0 million tranches, or the original HC Royalty loan agreement. We drew down the first tranche in the amount of $25.0 million in December 2012 upon signing the original HC Royalty loan agreement and we drew down the second tranche of $25.0 million in May 2013 as a result of our achievement of the milestone of U.S. approval of PROCYSBI. On July 1, 2014, we entered into an amended and restated loan agreement with HC Royalty as lender, or the HC Royalty loan agreement, under which we borrowed from HC Royalty a third $10.0 million tranche on July 23, 2014. The HC Royalty loan agreement includes a number of affirmative and negative covenants, including the use of commercially reasonable efforts to exploit PROCYSBI and 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. Our 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, 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 and related documents, the occurrence of a change of control of our Company or the occurrence of an uncured material adverse effect on our Company, or the occurrence of certain other specified events, could result in an event of default under the HC Royalty loan agreement that, if not cured or waived, could result in the acceleration of the payment of all of our indebtedness to HC Royalty and interest thereon. Under the terms of the security agreement, in an event of default, the lender could potentially take possession of, foreclose on, sell, assign or grant a license to use our pledged collateral and assign and transfer the pledged stock of certain of our subsidiaries. A default or material adverse effect or change of control would also trigger a prepayment penalty which would require us to pay a substantially higher amount due than the current balance of our

loan.

Credit risks from customers outside the U.S. may negatively affect our results of operations.

Any future sales of our products to government supported customers outside of the U.S. 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. For example, many governments in Europe are facing significant liquidity crises. If government reimbursement for future sales of PROCYSBI or our potential products in the EU is delayed or becomes unavailable, we may not be able to collect on amounts payable to us in reasonable time frames from such customers and our capital requirements will increase and our results of operations would be adversely affected.

Our business could be adversely affected by macroeconomic conditions.

Various macroeconomic factors could adversely affect our business and the results of our operations and financial condition, including changes in inflation, interest rates, foreign currency exchange rates and overall economic conditions and uncertainties, including those resulting from conditions in the global financial markets and business and economic conditions. For instance, if inflation or other factors were to significantly increase our business costs, it may not be feasible to increase the price of PROCYSBI or other future products due to the process by which healthcare providers are reimbursed.

In the recent past, the U.S. credit and capital markets experienced historic dislocations and a massive liquidity crisis which 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 negatively impact 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 adversely affect our business and results of operations.

Any product sales could be reduced by imports from countries where our product candidates are available at lower prices.

Even though we have FDA approval of PROCYSBI, our recognized product sales in the U.S. may be reduced if PROCYSBI is imported into the U.S. from lower priced markets, whether legally or illegally. In the U.S., 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 U.S. If such legislation were enacted, our potential future revenues could be reduced.

Our future international sales and operating expenses will be subject to fluctuations in currency exchange rates.

As we continue with the commercial launch of PROCYSBI in Germany and initiate launches in other countries in the EU and in other countries outside the U.S., a portion of our business will be conducted in currencies other than our reporting currency, the U.S. dollar. We will 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 will likely cause foreign currency translation gains and losses in the future. Because of the number of currencies that may be involved, the variability of currency exposures and the potential volatility of currency exchange rates, we may suffer significant foreign currency translation and transaction losses in the future due to the effect of exchange rate fluctuations.

Our future success depends, in part, on the continued services of our management team.

Our success is dependent in part upon the availability of our senior executive officers, including Christopher M. Starr, Ph.D., Chief Executive Officer; Julie Anne Smith, Chief Operating Officer; Georgia Erbez, Chief Financial Officer and Ted Daley, Chief Business Officer. The loss or unavailability to us of any of these individuals or key research and

development personnel, and particularly if lost to competitors, could have a material adverse effect on our business, prospects, financial condition and results of operations. We do not have key-man insurance on any of our employees.

There is no assurance that we will be able to retain key employees or consultants. There is intense competition for qualified scientists and managerial personnel from numerous pharmaceutical and biotechnology companies, as well as from academic and government organizations, research institutions and other entities. If

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key employees terminate their employment, or if insufficient numbers of qualified employees are retained, or are not available via recruitment, to maintain effective operations, our development activities might be adversely affected, management s attention might be diverted from managing our operations to hiring suitable replacements and our business might suffer. In addition, we might not be able to locate suitable replacements for any key employees that terminate their employment with us and we may not be able to offer employment to potential replacements on reasonable terms, which could negatively impact our product candidate development timelines and may adversely affect our future revenues and financial condition.

In addition to our employees, we rely and will continue to rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development strategy. All of our consultants and advisors will be employed by other employers or be self-employed, and will have commitments to or consulting or advisory contracts with other entities that may limit their availability to us.

If we do not achieve our projected development and commercialization goals in the time frames we expect and announce, the price of our common stock may decline.

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 various EU countries and other territories, commencement or completion of scientific studies and clinical trials, and the submission of regulatory filings.

From time to time, we may publicly announce the estimated timing of some of these milestones. All of these milestones will be based on a variety of assumptions. The actual timing of these milestones can vary dramatically compared to our estimates, in many cases for reasons beyond our control. For example, clinical trials may be delayed due to factors such as IRB approvals, qualification of clinical sites, scheduling conflicts with participating clinicians and clinical institutions and the rate of patient enrollment. In most circumstances, we rely on academic institutions, major medical institutions, governmental research organizations (U.S. or internationally based), clinical research organizations or CMOs to conduct, supervise or monitor some or all aspects of clinical trials involving our product candidates. We will have limited control over the timing and other aspects of these clinical trials. Furthermore, our ability to launch commercial sales of PROCYSBI in various countries in the EU is subject to the timely completion of reimbursement and pricing negotiations with various governmental entities in the EU, which process can be lengthy and uncertain. See also the risk factors titled The amount of our product sales of PROCYSBI in the EU is dependent upon the pricing and reimbursement guidelines adopted in each of the various countries in the EU, which levels may be below our current expectations and Our reliance on third parties may result in delays in completing, or a failure to complete, preclinical testing, clinical trials or regulatory marketing submissions.

If we do not meet the milestones 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 product development and commercialization goals and, as a result, the price of our common stock may decline.

Our executive offices and laboratory facility are located near known earthquake fault zones, and the occurrence of an earthquake or other catastrophic disaster could cause damage to our facility and equipment, or that of our third-party manufacturers or single-source suppliers, which could materially impair our ability to continue our product development programs.

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 the CMOs and our single-source suppliers

of raw materials and critical services are also vulnerable to damage from other types of disasters, including fires, storms, floods, power losses and similar events. If such a disaster were to occur, our ability to continue our product development programs or product commercialization activities 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.

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Risks Related to Intellectual Property and Competition

If we are unable to protect our proprietary technology, we may not be able to compete as effectively and our business and financial prospects may be harmed.

Where possible, we seek patent protection for certain aspects of our technology. Patent protection may not be available for some of the drug product candidates we are developing. If we must spend extraordinary time and money protecting our patents, designing around patents held by others or licensing, potentially for large fees, patents or other proprietary rights held by others, our business and financial prospects may be harmed.

The patent positions of biopharmaceutical products are complex and uncertain.

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. However, these patents and patent applications do not ensure the protection of our intellectual property for a number of reasons, including the following:

- We do not know whether our patent applications will result in issued patents. For example, we may not have developed a method for treating a disease before others developed similar methods;

- Competitors may interfere with our patent process in a variety of ways. Competitors may claim that they invented the claimed invention prior to us, or file patent applications before we do. Competitors may also claim that we are infringing on their patents and therefore cannot practice our technology as claimed under our patents, if issued. Competitors may also contest our patents, if issued, by showing the patent examiner that the invention was not original, was not novel or was obvious. In litigation, a competitor could claim that our patents, if issued, are not valid for a number of reasons. If a court agrees, we would lose that patent. As a Company, we have no meaningful experience with competitors interfering with our patents or patent applications;

- Enforcing patents is expensive and may absorb significant management time. Management would spend less time and resources on developing drug product candidates. The processes of defending patents and related intellectual property could increase our operating expenses and delay product programs; and

- Receipt of a patent may not provide practical protection. If we receive a patent with a narrow scope, then it will be easier for competitors to design products that do not infringe on our patent.

In addition, competitors also seek patent protection for their technology. Due to the number of patents in our field of technology, we cannot be certain that we do not infringe on those patents or that we will not infringe on patents granted in the future. If a patent holder believes our drug product candidate infringes on its patent, the patent holder may sue us even if we have received patent protection for our technology. If someone else claims we infringe on their technology, we would face a number of issues, including the following:

- Defending a lawsuit takes significant time is typically very expensive;

If a court decides that our drug product candidate infringes on the competitor s patent, we may have to pay substantial damages for past infringement;

A court may prohibit us from selling or licensing the drug product candidate unless the patent holder licenses the patent to us. The patent holder is not required to grant us a license. If a license is available, we may have to pay substantial royalties or grant cross licenses to our patents; and

Redesigning our drug product candidates so we do not infringe may not be possible or practical and could require substantial funds and time.

Our trade secrets may not be adequately protected. While we use reasonable efforts to protect our trade secrets, our employees or consultants may unintentionally or willfully disclose our information to competitors. Enforcing a claim that someone else 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 U.S. are sometimes less willing to protect trade secrets. Our competitors may independently develop equivalent knowledge, methods and know-how. We may also support and collaborate in research conducted by government

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organizations, hospitals, universities or other educational institutions. These research partners may be unwilling to grant us any exclusive rights to technology or products derived from these collaborations prior to entering into the relationship. 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.

If we are limited in our ability to utilize acquired or licensed technologies, we may be unable to develop, out-license, market and sell our product candidates, which could prevent new product introductions and/or cause delayed 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. These agreements may be terminated, and all rights to the technologies and product candidates will be lost, if we fail to perform our obligations under these agreements and licenses in accordance with their terms including, but not limited to, our ability to fund all payments due under such agreements. Our inability to continue to maintain these technologies could adversely affect our business, financial condition and results of operations. In addition, our business strategy depends on the successful development of licensed and acquired technologies into commercial products, and, 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, delay new product introductions, and/or adversely affect our reputation, any of which could have a material adverse effect on our business, financial condition and results of operations.

If our licensing agreements are terminated, we will lose the right to use or exploit our owned and licensed technologies.

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 which permit the licensor to terminate our license under certain circumstances, including if we materially breach our obligations and fail to remedy the breach within permitted cure periods. 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 relating to those respective technologies and it could impact our ability to market PROCYSBI or continue our development programs of RP103 in other clinical indications. If this happens our financial condition and results of operations will be adversely affected, and we may have to cease our operations.

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 similar technologies that we are pursuing and are developing pharmaceutical products that are competitive with PROCYSBI or our drug product candidates. Many of our pharmaceutical competitors who are 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.

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 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.

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If our agreements with employees, consultants, advisors, suppliers and corporate partners fail to protect our intellectual property, proprietary information or trade secrets, it could have a significant adverse effect on us.

We have taken steps to protect our intellectual property and proprietary technology, by entering into confidentiality agreements and intellectual property assignment agreements with our employees, consultants, advisors and corporate and educational institution partners. 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 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. Furthermore, the laws of some foreign countries may not protect our intellectual property rights to the same extent as do the laws of the U.S.

Risks Related to Our Financial Position and Capital Requirements

Our commercialization efforts and clinical development programs will require substantial future funding which will impact our operational and financial condition.

Excluding PROCYSBI for cystinosis, it will take a substantial period of time before we are able to develop our other drug product candidates into marketable drug products, if at all. The marketing and sales efforts for PROCYSBI and any future approved products, obtaining adequate reimbursement for products and our product development programs will require substantial additional capital, arising from costs to:

conduct research, preclinical testing and human studies and clinical trials;

establish or contract for pilot scale and commercial scale manufacturing processes and facilities;

market and distribute PROCYSBI and any future approved products; and

establish and develop quality control, manufacturing, regulatory, medical, pharmacovigilance, distribution, marketing, sales, finance and administrative capabilities to support these programs.

Our future operating and capital needs will depend on many factors, including:

the effectiveness of our commercialization activities;

the scope and results of preclinical testing and human clinical trials;

the pace of scientific progress in our research and development programs and the magnitude of these programs;

our ability to obtain, and the time and costs involved in obtaining, regulatory approvals;

the cost of manufacturing scale-up for new product candidates;

our ability to prosecute, maintain and enforce, and the time and costs involved in preparing, filing, prosecuting, maintaining and enforcing, patent claims;

competing technological and market developments;

our ability to establish additional collaborations; and

changes in our existing collaborations.

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 U.S. and EU, our efforts to commercialize any future approved products, the success of our research initiatives, regulatory approvals, the timing of events outside our direct control, such as negotiations with healthcare 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.

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Significant additional funds from outside financing sources will be required to support our operations. If we are unable to obtain them on acceptable terms, we may be required to cease or reduce further development of PROCYSBI and our other drug product programs, to sell some or all of our technology or assets, to merge with another entity or to cease operations.

If we fail to obtain the capital necessary to fund our operations, our operational and financial results will be adversely affected.

As of June 30, 2014, we had an accumulated deficit of approximately $232.9 million. In addition to the proceeds from this offering, we will need to raise additional capital and/or generate significant revenue at profitable levels to fund our development and commercialization programs in accordance with our plans.

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 expenses for PROCYSBI, which would have a material adverse effect on our financial condition and operating results.

While we believe that based upon our projected PROCYSBI sales and planned operations, our cash and cash equivalents of $58.1 million as of June 30, 2014 will be sufficient to meet our projected operational requirements and obligations through at least through the first half of 2015, in addition to this offering, in the future, we may 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. 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 the U.S., the execution of our launch of PROCYSBI in Europe and the general condition of the financial markets. 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 expenses for PROCYSBI. If such actions are required, our financial condition and operating results will be adversely affected and our future value may be significantly reduced.

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 may require a substantial portion, or all, of our available cash to be dedicated to the service of these debt obligations. The loan bears interest at an annual fixed rate of 8.0% and a synthetic royalty based on the amount of PROCYSBI and other future approved product net revenues in a calendar year, and such interest and royalty are payable quarterly. Principal payments under the HC Royalty loan agreement will become due beginning in June 2015.

There is 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. 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, and we may be forced to restructure our indebtedness or raise additional capital through the issuance of equity or debt instruments in addition to this offering. We cannot ensure 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. In addition, the terms of the HC Royalty loan agreement may limit our ability to pursue any of these financing alternatives and these alternatives 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, take possession of, foreclose on, sell, assign or grant a license to use, our pledged collateral and assign and transfer the pledged stock of our subsidiaries. A default or material adverse effect or change of control would also trigger a prepayment penalty which would require us to pay a substantially higher amount due than the current balance of our loan. This could have a material adverse impact on our financial condition and results of operations.

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USE OF PROCEEDS

We expect to use the net proceeds from the offering to fund our commercial and pre-commercial efforts, our clinical and preclinical development programs and other general corporate purposes. The amounts and timing of these expenditures will depend on a number of factors, such as: the success of commercial sales of PROCYSBI in the U.S. and EU; the timing of additional regulatory approvals, if any; the progress of our commercial and pre-commercial efforts with respect to RP103 for the potential treatment of HD, NA and Leigh syndrome; the progress of our research and development programs for ALDH2 deficiency and our HepTide and other pre-clinical programs; and technological advances and the competitive environment for all of our drug candidates. Pending these uses, we intend to invest the net proceeds in short-term, investment-grade, interest-bearing securities.

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DILUTION

Purchasers of common stock offered by this prospectus supplement and the accompanying prospectus will suffer immediate and substantial dilution in the net tangible book value per share of common stock. Our net tangible book value as of June 30, 2014 was approximately $12.2 million, or approximately $0.20 per share of common stock. Net tangible book value per share represents the amount of total tangible assets less total liabilities other than warrant liabilities (non-cash), divided by the number of shares of our common stock outstanding as of June 30, 2014.

Dilution in net tangible book value per share represents the difference between the amount per share paid by purchasers in this offering and the net tangible book value per share of our common stock immediately after this offering. After giving effect to the assumed sale of shares of our common stock in the aggregate amount of $46.2 million at an assumed offering price of $11.44 per share, the last reported sale price of our common stock on August 19, 2014, and after deduction of commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of June 30, 2014 would have been approximately $56.9 million, or $0.85 per share of common stock. This represents an immediate increase in net tangible book value of $0.65 per share of common stock to our existing stockholders and an immediate dilution in net tangible book value of $10.59 per share of common stock to investors participating in this offering. The following table illustrates this per share dilution:

Assumed offering price per share		$ 11.44
Net tangible book value per share as of June 30, 2014	$ 0.20	
Increase per share attributable to this offering	0.65	
As adjusted net tangible book value per share after the offering as of June 30, 2014, after giving effect to this offering		0.85
Net dilution per share to investors participating in this offering		$ 10.59

Changes in the assumed offering price of $11.44 per share would not affect our as adjusted net tangible book value after this offering because this offering is currently limited to $46.2 million. However, each $1.00 increase (decrease) in the assumed offering price of $11.44 per share would increase (decrease) our as adjusted per share net tangible book value after this offering by approximately $0.94 per share, and the dilution per share to new investors by approximately $11.53 per share, assuming that the aggregate dollar amount of shares offered by us, as set forth above, remains at $46.2 million and after deducting the commissions and estimated offering expenses payable by us. We may also increase or decrease the aggregate dollar amount of shares we are offering from the amount set forth above. The information discussed above is illustrative only and will adjust based on the actual offering price, the actual number of shares that we offer and sell in this offering, and other terms of this offering determined at the time of each offer and sale.

The information above and in the foregoing table is based upon 62.7 million shares of our common stock outstanding as of June 30, 2014. The information above and in the foregoing table is as of June 30, 2014 and excludes:

- 10.0 million shares of our common stock issuable upon the exercise of options outstanding under our stock option plans as of June 30, 2014 at a weighted average exercise price of $7.72 per share;

1.7 million shares of our common stock available for future issuance under our stock option plans as of June 30, 2014; and

0.3 million shares of our common stock issuable upon exercise of outstanding warrants as of June 30, 2014 at a weighted average exercise price of $4.54 per share.

The information above and in the foregoing table also excludes $60.0 million aggregate principal amount of 8.0% convertible senior notes due 2019 that we issued in July 2014. The convertible senior notes are convertible at the option of the holder at a conversion rate of 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 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. The maximum number of shares of common stock issuable upon conversion of the notes is 3,428,571.

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PLAN OF DISTRIBUTION

We have entered into a second amended and restated sales agreement with Cowen, under which we may issue and sell from time to time up to $46,193,473.43 of our common stock through Cowen as our sales agent. These shares are in addition to $53,806,526.57 of shares of common stock previously sold pursuant to the sales agreement, as amended and restated on July 3, 2013, and offered by the prospectus supplement dated April 30, 2012, as amended on July 3, 2013 (to prospectus dated February 3, 2012), under a shelf registration statement on Form S-3 (Registration No. 333-179215). Sales of our common stock, if any, will be made at market prices by any method that is deemed to be an at the market offering as defined in Rule 415 under the Securities Act, including sales made directly on The Nasdaq Global Market and any other trading market for our common stock, and sales to or through a market maker other than on an exchange.

Cowen will offer our common stock subject to the terms and conditions of the second amended and restated sales agreement on a daily basis or as otherwise agreed upon by us and Cowen. We will designate the maximum amount of common stock to be sold through Cowen on a daily basis or otherwise determine such maximum amount together with Cowen. Subject to the terms and conditions of the second amended and restated sales agreement, Cowen will use its commercially reasonable efforts to sell on our behalf all of the shares of common stock requested to be sold by us. We may instruct Cowen not to sell common stock if the sales cannot be effected at or above the price designated by us in any such instruction. Cowen or we may suspend the offering of our common stock being made through Cowen under the second amended and restated sales agreement upon proper notice to the other party. Cowen and we each have the right, by giving written notice as specified in the second amended and restated sales agreement, to terminate the second amended and restated sales agreement in each party s sole discretion at any time.

The aggregate compensation payable to Cowen as sales agent equals 3.0% of the gross sales price of the shares sold through it pursuant to the second amended and restated sales agreement. We estimate that the total expenses of the offering payable by us, excluding commissions payable to Cowen under the second amended and restated sales agreement, will be approximately $150,000.

The remaining sales proceeds, after deducting any expenses payable by us and any transaction fees imposed by any governmental, regulatory, or self-regulatory organization in connection with the sales, will equal our net proceeds for the sale of such common stock.

Cowen will provide written confirmation to us following the close of trading on The Nasdaq Global Market as applicable, each day in which common stock is sold through it as sales agent under the second amended and restated sales agreement. Each confirmation will include the number of shares of common stock sold through it as sales agent on that day, the gross sales price per share, the net proceeds to us and the compensation payable by us to Cowen.

We will report at least quarterly the number of shares of common stock sold through Cowen under the second amended and restated sales agreement, the net proceeds to us and the compensation paid by us to Cowen in connection with the sales of common stock.

Settlement for sales of common stock will occur, unless the parties agree otherwise, on the third business day that is also a trading day following the date on which any sales were made in return for payment of the net proceeds to us. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

In connection with the sales of our common stock on our behalf, Cowen may be deemed to be an underwriter within the meaning of the Securities Act, and the compensation paid to Cowen may be deemed to be underwriting commissions or discounts. We have agreed in the second amended and restated sales agreement to provide

indemnification and contribution to Cowen against certain liabilities, including liabilities under the Securities Act. As sales agent, Cowen will not engage in any transactions that stabilizes our common stock.

Our common stock is listed on The Nasdaq Global Market and trades under the symbol RPTP. The transfer agent of our common stock is American Stock Transfer & Trust Company, LLC.

Cowen and/or its affiliates have provided, and may in the future provide, various investment banking and other financial services for us for which services they have received and, may in the future receive, customary fees.

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LEGAL MATTERS

Latham & Watkins LLP, Menlo Park, California will pass upon the validity of the securities being offered by this prospectus supplement. Certain matters will be passed upon for Cowen by Goodwin Procter LLP, New York, New York.

EXPERTS

The consolidated balance sheets as of December 31, 2013 and 2012, and the related consolidated statements of operations and comprehensive loss, stockholders equity (deficit) and cash flows for the year ended December 31, 2013 and for the four-month period ended December 31, 2012, the financial statement schedule, and management s assessment of the effectiveness of internal control over financial reporting, that are incorporated by reference in this prospectus supplement and elsewhere in the registration statement of which this prospectus supplement forms a part have been so incorporated by reference in reliance upon the reports of Grant Thornton LLP, independent registered public accountants, upon the authority of said firm as experts in accounting and auditing. The consolidated statements of operations and comprehensive loss, stockholders equity (deficit) and cash flows for the fiscal years ended August 31, 2012 and 2011, the financial statement schedule, and management s assessment of the effectiveness of internal control over financial reporting, that are incorporated by reference in this prospectus supplement and elsewhere in the registration statement of which this prospectus supplement forms a part have been so incorporated by reference in reliance upon the reports of Burr Pilger Mayer, Inc., independent registered public accountants, upon the authority of said firm as experts in accounting and auditing.

With respect to the unaudited interim financial information for the quarters ended March 31, 2013, June 30, 2013 and September 30, 2013, incorporated by reference in this prospectus supplement and elsewhere in the registration statement of which this prospectus supplement forms a part, Grant Thornton LLP has reported that they have applied limited procedures in accordance with professional standards for a review of such information. However, their separate reports thereon state that they did not audit and they do not express an opinion on that interim financial information. Accordingly, the degree of reliance on their report on such information should be restricted in light of the limited nature of the review procedures applied. In addition, Grant Thornton LLP is not subject to the liability provisions of Section 11 of the Securities Act of 1933 for their report on the unaudited interim financial information because that report is not a report or a part of the registration statement of which this prospectus supplement forms a part prepared or certified by the accountants within the meaning of the Sections 7 and 11 of that Act.

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WHERE YOU CAN FIND MORE INFORMATION; INCORPORATION BY REFERENCE

Available Information

We file reports, proxy statements and other information with the SEC. Information filed with the SEC by us can be inspected and copied at the Public Reference Room maintained by the SEC at 100 F Street, N.E., Washington, D.C. 20549. You may also obtain copies of this information by mail from the Public Reference Section of the SEC at prescribed rates. Further information on the operation of the SEC s Public Reference Room in Washington, D.C. can be obtained by calling the SEC at 1-800-SEC-0330. The SEC also maintains a website that contains reports, proxy and information statements and other information about issuers, such as us, who file electronically with the SEC. The address of that website is http://www.sec.gov.

Our web site address is http://www.raptorpharma.com. The information on our web site, however, is not, and should not be deemed to be, a part of this prospectus supplement.

This prospectus supplement is part of a registration statement that we filed with the SEC and does not contain all of the information in the registration statement. The full registration statement may be obtained from the SEC or us, as provided below. Whenever a reference is made in this prospectus supplement to a contract or other document, the reference is only a summary and you should refer to the exhibits that are a part of the registration statement for a copy of the contract or other document. You may review a copy of the registration statement at the SEC s Public Reference Room in Washington, D.C., as well as through the SEC s website, as provided above.

Incorporation by Reference

The SEC s rules allow us to incorporate by reference information into this prospectus supplement, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is deemed to be part of this prospectus supplement, and subsequent information that we file with the SEC will automatically update and, if applicable, supersede that information. Any statement contained in a previously filed document incorporated by reference will be deemed to be modified or superseded for purposes of this prospectus supplement to the extent that a statement contained in this prospectus supplement or any related free writing prospectus that we may provide or any subsequently filed document that is incorporated by reference in this prospectus supplement modifies or replaces that statement.

We incorporate by reference our documents listed below and any future filings made by us with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, which we refer to as the Exchange Act in this prospectus supplement, between the date of this prospectus supplement and the termination of the offering of the securities described in this prospectus supplement. We are not, however, incorporating by reference any documents or portions thereof or exhibits thereto, whether specifically listed below or filed in the future, that are not deemed filed with the SEC, including our Compensation Committee report and performance graph or any information furnished pursuant to Items 2.02 or 7.01 of Form 8-K or related exhibits furnished pursuant to Item 9.01 of Form 8-K.

This prospectus supplement incorporates by reference the documents set forth below that have previously been filed with the SEC:

Our Transition Report on Form 10-KT for the four-month period ended December 31, 2012, originally filed with the SEC on March 14, 2013, as amended by Amendment No. 1 on Form 10-KT/A on June 19, 2013 and Amendment No. 2 on Form 10-KT/A on May 12, 2014;

Our Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2013, filed with the SEC on August 9, 2013, as amended by Amendment No. 1 on Form 10-Q/A on June 19, 2013 and Amendment No. 2 on Form 10-Q/A on May 12, 2014;

Our Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2013, filed with the SEC on May 8, 2013, as amended by Amendment No. 1 on Form 10-Q/A on May 12, 2014;

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Our Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2013, filed with the SEC on November 7, 2013, as amended by Amendment No. 1 on Form 10-Q/A on May 12, 2014;

Our Annual Report on Form 10-K for the year ended December 31, 2013, filed with the SEC on March 17, 2014;

Our Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2014, filed with the SEC on May 9, 2014;

Our Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2014, filed with the SEC on August 7, 2014;

Our Current Reports on Form 8-K filed with the SEC on January 14, 2014, January 22, 2014, February 24, 2014, February 26, 2014, July 3, 2014, July 8, 2014, July 29, 2014, August 4, 2014, August 5, 2014 and August 21, 2014;

The description of our Series A Participating Preferred Stock contained in the Registration Statement on Form 8-A filed on May 16, 2005 (File No. 000-25571), as amended on May 12, 2014, pursuant to Section 12(g) of the Exchange Act, including any amendment or report filed for the purpose of updating such description.

All reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the termination of this offering, excluding any documents or portions thereof or exhibits thereto that are furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus supplement and deemed to be part of this prospectus supplement from the date of the filing of such reports and documents.

You may request a free copy of any of the documents incorporated by reference in this prospectus supplement (other than exhibits, unless they are specifically incorporated by reference in the documents) by writing or telephoning us at the following address:

Raptor Pharmaceutical Corp.

7 Hamilton Landing, Suite 100

Novato, CA 94949

(415) 408-6200

Attn: Secretary

Exhibits to the filings will not be sent, however, unless those exhibits have specifically been incorporated by reference in this prospectus and any accompanying prospectus supplement.

Trademark Notice

Raptor, our logos and all of our product candidates and trade names are our registered trademarks or our trademarks in the United States and in other select countries. Other third-party logos and product/trade names are registered trademarks or trade names of their respective companies.

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PROSPECTUS

Raptor Pharmaceutical Corp.

Common Stock

Preferred Stock

Warrants

Units

We may offer and sell the securities identified above from time to time in one or more offerings. This prospectus provides you with a general description of the securities.

Each time we offer and sell securities, we will provide a supplement to this prospectus that contains specific information about the offering and the amounts, prices and terms of the securities. The supplement may also add, update or change information contained in this prospectus with respect to that offering. You should carefully read this prospectus and the applicable prospectus supplement before you invest in any of our securities.

We may offer and sell the securities described in this prospectus and any prospectus supplement to or through one or more underwriters, dealers and agents, or directly to purchasers, or through a combination of these methods. If any underwriters, dealers or agents are involved in the sale of any of the securities, their names and any applicable purchase price, fee, commission or discount arrangement between or among them will be set forth, or will be calculable from the information set forth, in the applicable prospectus supplement. See the sections of this prospectus entitled About this Prospectus and Plan of Distribution for more information. No securities may be sold without delivery of this prospectus and the applicable prospectus supplement describing the method and terms of the offering of such securities.

INVESTING IN OUR SECURITIES INVOLVES RISKS. SEE THE RISK FACTORS ON PAGE 6 OF THIS PROSPECTUS AND ANY SIMILAR SECTION CONTAINED IN THE APPLICABLE PROSPECTUS SUPPLEMENT CONCERNING FACTORS YOU SHOULD CONSIDER BEFORE INVESTING IN OUR SECURITIES.

Our common stock is listed on The NASDAQ Global Market under the symbol RPTP. On May 9, 2014, the last reported sale price of our common stock on The NASDAQ Global Market was $7.83 per share.

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

The date of this prospectus is May 12, 2014.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the U.S. Securities and Exchange Commission, or the SEC, as a well-known seasoned issuer as defined in Rule 405 under the Securities Act of 1933, as amended, using a shelf registration process. By using a shelf registration statement, we may sell securities from time to time and in one or more offerings as described in this prospectus. Each time that we offer and sell securities, we will provide a prospectus supplement to this prospectus, and may provide one or more free writing prospectuses, that contain specific information about the securities being offered and sold and the specific terms of that offering. The prospectus supplement and any related free writing prospectus that we may provide may also add, update or change information contained in this prospectus with respect to that offering. If there is any inconsistency between the information in this prospectus and the applicable prospectus supplement or any related free writing prospectus that we may provide, you should rely on that prospectus supplement or such free writing prospectus, as the case may be. Before purchasing any securities, you should carefully read this prospectus, the applicable prospectus supplement and any related free writing prospectus that we may provide, together with the documents incorporated by reference herein as described under the heading Where You Can Find More Information; Incorporation by Reference.

We have not authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We will not make an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus, the applicable prospectus supplement to this prospectus and any related free writing prospectus that we may provide is accurate as of the date on its respective cover, and that any information incorporated by reference is accurate only as of the date of the document incorporated by reference, unless we indicate otherwise. Our business, financial condition, results of operations and prospects may have changed since those dates.

When we refer to Raptor Pharmaceutical, we, our, us and the Company in this prospectus, we mean Raptor Pharmaceutical Corp. (including its predecessors) and its consolidated subsidiaries, unless otherwise specified. When we refer to you, we mean the prospective purchasers of the applicable securities.

This prospectus and any accompanying prospectus supplement, including the information incorporated by reference into this prospectus and any accompanying prospectus supplement, and any free writing prospectuses we have authorized for use in connection with any offering, include trademarks, service marks and trade names owned by us or others companies. All trademarks, service marks and trade names included or incorporated by reference into this prospectus and any accompanying prospectus supplement, and any free writing prospectuses we have authorized for use in connection with any offering, are the property of their respective owners.

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NOTE REGARDING MARKET DATA

We obtained the statistical data, market data and other industry data and forecasts that appears or may appear in this prospectus, any related prospectus supplement or any related free writing prospectus that we may provide and the documents incorporated by reference in this prospectus from sources such as market research reports, publicly available information, industry publications and estimates made by our management. While we believe that this data and these forecasts are reliable, we have not independently verified this information, and we do not make any representation as to the accuracy of this information. We have not sought the consent of the sources to refer to their reports or data appearing or incorporated by reference in this prospectus or any related prospectus supplement or any related free writing prospectus that we may provide.

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WHERE YOU CAN FIND MORE INFORMATION; INCORPORATION BY REFERENCE

Available Information

We file reports, proxy statements and other information with the SEC. Information filed with the SEC by us can be inspected and copied at the Public Reference Room maintained by the SEC at 100 F Street, N.E., Washington, D.C. 20549. You may also obtain copies of this information by mail from the Public Reference Section of the SEC at prescribed rates. Further information on the operation of the SEC s Public Reference Room in Washington, D.C. can be obtained by calling the SEC at 1-800-SEC-0330. The SEC also maintains a website that contains reports, proxy and information statements and other information about issuers, such as us, who file electronically with the SEC. The address of that website is *http://www.sec.gov*.

Our web site address is *http://www.raptorpharma.com*. The information on our web site, however, is not, and should not be deemed to be, a part of this prospectus.

This prospectus and any prospectus supplement are part of a registration statement that we filed with the SEC and do not contain all of the information in the registration statement. The full registration statement may be obtained from the SEC or us, as provided below. Documents establishing the terms of the offered securities are or may be filed as exhibits to the registration statement or as exhibits to a document incorporated by reference in the registration statement. Statements in this prospectus, any prospectus supplement or any related free writing prospectus that we may provide about these documents are summaries and each statement is qualified in all respects by reference to the document to which it refers. You should refer to the actual documents for a more complete description of the relevant matters. You may inspect a copy of the registration statement at the SEC s Public Reference Room in Washington, D.C. or through the SEC s website, as provided above.

Incorporation by Reference

The SEC s rules allow us to incorporate by reference information into this prospectus, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is deemed to be part of this prospectus, and subsequent information that we file with the SEC will automatically update and, if applicable, supersede that information. Any statement contained in a previously filed document incorporated by reference will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus, any related prospectus supplement or any related free writing prospectus that we may provide or any subsequently filed document that is incorporated by reference in this prospectus modifies or replaces that statement.

We incorporate by reference our documents listed below and any future filings made by us with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, which we refer to as the Exchange Act in this prospectus, between the date of this prospectus and the termination of the offering of the securities described in this prospectus. We are not, however, incorporating by reference any documents or portions thereof or exhibits thereto, whether specifically listed below or filed in the future, that are not deemed filed with the SEC, including our Compensation Committee report and performance graph or any information furnished pursuant to Items 2.02 or 7.01 of Form 8-K or related exhibits furnished pursuant to Item 9.01 of Form 8-K.

This prospectus and any accompanying prospectus supplement incorporate by reference the documents set forth below that have previously been filed with the SEC:

Our Transition Report on Form 10-KT for the four month period ended December 31, 2012, originally filed with the SEC on March 14, 2013, as amended by Amendment No. 1 on Form 10-KT/A on June 19, 2013 and Amendment No. 2 on Form 10-KT/A on May 12, 2014;

Our Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2013, filed with the SEC on August 9, 2013, as amended by Amendment No. 1 on Form 10-Q/A on June 19, 2013 and Amendment No. 2 on Form 10-Q/A on May 12, 2014;

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Our Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2013, filed with the SEC on May 8, 2013, as amended by Amendment No. 1 on Form 10-Q/A on May 12, 2014;

Our Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2013, filed with the SEC on November 7, 2013, as amended by Amendment No. 1 on Form 10-Q/A on May 12, 2014;

Our Annual Report on Form 10-K for the year ended December 31, 2013, filed with the SEC on March 17, 2014;

Our Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2014, filed with the SEC on May 9, 2014;

Our Current Reports on Form 8-K filed with the SEC on January 14, 2014, January 22, 2014, February 24, 2014 and February 26, 2014;

The description of our Series A Participating Preferred Stock contained in the Registration Statement on Form 8-A filed on May 16, 2005 (File No. 000-25571), as amended on May 12, 2014, pursuant to Section 12(g) of the Exchange Act, including any amendment or report filed for the purpose of updating such description.

All reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the termination of this offering, excluding any documents or portions thereof or exhibits thereto that are furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus and deemed to be part of this prospectus from the date of the filing of such reports and documents.

You may request a free copy of any of the documents incorporated by reference in this prospectus (other than exhibits, unless they are specifically incorporated by reference in the documents) by writing or telephoning us at the following address:

Raptor Pharmaceutical Corp.

5 Hamilton Landing, Suite 160

Novato, CA 94949

(415) 408-6200

Attn: Secretary

Exhibits to the filings will not be sent, however, unless those exhibits have specifically been incorporated by reference in this prospectus and any accompanying prospectus supplement.

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THE COMPANY

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

Our first product, PROCYSBI® (cysteamine bitartrate) delayed-release capsules, or PROCYSBI, received marketing approval from the U.S. Food and Drug Administration on April 30, 2013 for the management of nephropathic cystinosis, a rare, life-threatening metabolic lysosomal storage disorder, in adults and children six years and older. The European equivalent, PROCYSBI® gastro-resistant hard capsules of cysteamine (as mercaptamine bitartrate), received marketing authorization on September 6, 2013 from the European Commission, or EC, as an orphan medicinal product for the management of proven nephropathic cystinosis for marketing in the European Union, or EU. PROCYSBI® received seven years and ten years of market exclusivity as an orphan drug in the U.S. and the EU, respectively. We commenced commercial sales of PROCYSBI® in the U.S. in June 2013 and in Germany in April 2014.

Raptor Pharmaceutical Corp. was initially incorporated in Nevada on July 29, 1997 as Axonyx Inc. In October 2006, Axonyx Inc. and its then-wholly-owned subsidiary completed a reverse merger, business combination with TorreyPines Therapeutics, Inc., reincorporated in Delaware and changed its name to TorreyPines Therapeutics, Inc. In September 2009, we and our wholly-owned subsidiary completed a reverse merger, business combination with Raptor Pharmaceuticals Corp. pursuant to which Raptor Pharmaceuticals Corp. became our wholly-owned subsidiary. Immediately prior to the merger, we changed our corporate name from TorreyPines Therapeutics, Inc. to Raptor Pharmaceutical Corp.

Our principal executive offices are located at 5 Hamilton Landing, Suite 160, Novato, CA 94949, and our telephone number is (415) 408-6200.

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RISK FACTORS

Investment in any securities offered pursuant to this prospectus and the applicable prospectus supplement involves risks. You should carefully consider the risk factors incorporated by reference from our most recent Annual Report on Form 10-K, and any subsequent Quarterly Reports on Form 10-Q and Current Reports on Form 8-K (in each case including all amendments thereto), and all other information contained or incorporated by reference into this prospectus, as updated by our subsequent filings under the Exchange Act, and the risk factors and other information contained in the applicable prospectus supplement and any related free writing prospectus that we may provide before acquiring any of such securities. The occurrence of any of these risks might cause you to lose all or part of your investment in the offered securities.

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USE OF PROCEEDS

We intend to use the net proceeds from the sale of the securities as set forth in the applicable prospectus supplement.

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RATIO OF EARNINGS TO FIXED CHARGES

The following table sets forth the dollar amount of the coverage deficiency for each of the periods presented. As the ratios of earnings to fixed charges indicate less than one-to-one coverage in each of the periods presented, we have provided the coverage deficiency amounts for those periods. You should read these figures in connection with our consolidated financial statements, including the notes to those statements, incorporated by reference in this prospectus. See Exhibit 12.1 hereto for additional detail regarding the computation of the deficiency of earnings to cover fixed charges.

	Year Ended December 31, 2013	Four Months Ended December 31, 2012	Years Ended August 31, 2012	2011	2010	2009	Three Months Ended March 31, 2014
				(in thousands)			
Deficiency of earnings to cover fixed charges (1)	$ (69,417)	$ (19,292)	$ (38,644)	$ (37,195)	$ (18,928)	$ (9,224)	$ (14,885)

(1) For purposes of computing the deficiency of earnings to fixed charges, earnings consist of reported net loss plus fixed charges. Fixed charges are the sum of Interest expense, amortization of debt costs, and portion of rental expense attributable to interest. Due to our net losses for each of the periods presented, earnings were insufficient to cover fixed charges for these periods

For the periods indicated above, we had no outstanding shares of preferred stock with required dividend payments. Therefore, the deficiency of earnings to fixed charges and preferred stock dividends are identical to the table above.

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DESCRIPTION OF CAPITAL STOCK

The following description of our capital stock is not complete and may not contain all the information you should consider before investing in our capital stock. This description is summarized from, and qualified in its entirety by reference to, our certificate of incorporation, as amended, our bylaws, as amended, and our Rights Agreement (as defined below), which have been publicly filed with the SEC. See Where You Can Find More Information; Incorporation by Reference.

Our authorized capital stock consists of:

- 150,000,000 shares of common stock, $0.001 par value; and
- 15,000,000 shares of preferred stock, $0.001 par value.

Common Stock

Dividends

Subject to any preferential rights to receive dividends of any outstanding shares of our preferred stock (including, if issued, our Series A participating preferred stock described below), the holders of our common stock will be entitled to receive, ratably in proportion to the number of shares of our common stock held by them, any dividends that may be declared on our common stock by our board of directors out of funds legally available for the payment of dividends.

Voting Rights

For the purpose of determining those stockholders entitled to vote at any meeting of our stockholders, except as otherwise provided by law, only persons in whose names shares of stock stand on our stock records on the applicable record date, as provided in our bylaws, as amended, shall be entitled to vote at any meeting of stockholders. Every person entitled to vote shall have the right to do so either in person, by remote communication, if applicable, or by an agent or agents authorized by a proxy granted in accordance with Delaware law. An agent so appointed need not be a stockholder. No proxy shall be voted after three (3) years from its date of creation unless the proxy provides for a longer period.

Each outstanding share of common stock will entitle the holder to one vote on each matter properly submitted to our stockholders for their vote; provided, however, that holders of common stock shall not be entitled to vote on any amendment to our certificate of incorporation, as amended, that relates solely to the terms of one or more outstanding series of our preferred stock if the holders of such affected series of preferred stock are entitled to vote thereon. The holders of our common stock are not entitled to cumulative voting rights in the election of our directors, which means that holders of a majority of the outstanding shares of our common stock will be entitled to elect all of our directors standing for election by holders of our common stock. In the event that shares of our Series A Participating Preferred Stock are issued, the Series A Participating Preferred Stock and our common stock will vote together as one class on all matters submitted to a vote of our stockholders as described below under Shareholder Rights Plan; Series A Participating Preferred Stock .

Our bylaws, as amended, provide that our stockholders have the power to adopt, amend or repeal our bylaws; provided, that in addition to any vote of the holders of any class or series of our stock required by law or by our certificate of incorporation, as amended, such action by stockholders shall require the affirmative vote of the holders of at least 66-2/3% of the voting power of all of the then-outstanding shares of our capital stock entitled to vote generally in the election of directors, voting together as a single class. Our board of directors also is empowered to amend our bylaws without the consent of our stockholders. In addition, our certificate of incorporation, as amended, and our bylaws, as amended, provide that a director may be removed at any time (a) with cause by the affirmative vote of the holders of a majority of the voting power of all then-outstanding shares of our capital stock entitled to vote at an election of directors or (b) without cause by the affirmative vote of the holders of $66^{2}/_{3}$% of the voting power of all then-outstanding shares of our capital stock entitled to vote at an election of directors.

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No Preemptive or Similar Rights

Our common stock is not entitled to preemptive or similar rights to acquire shares of our common stock or other securities and is not subject to conversion into other securities or redemption at our option or at the option of any holder.

Right to Receive Liquidation Distributions

If we voluntarily or involuntarily liquidate, dissolve or wind-up, the holders of our common stock will be entitled to receive, after payment of or provision for all of our debts and other liabilities and distribution in full of the preferential amounts, if any, to be distributed to the holders of any outstanding preferred stock, all of our remaining assets available for distribution, ratably in proportion to the number of shares of our common stock held by them.

Other

Our outstanding common stock is fully paid and non-assessable. The rights, preferences and privileges of holders of our common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of our preferred stock, which our board of directors may designate and issue in the future.

Transfer Agent

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC.

Preferred Stock

Our board of directors is authorized, without action by our stockholders, to provide for the issuance of shares of preferred stock in one or more series, and to fix the number of shares and to determine for each series such voting rights, if any, designations, preferences and relative, participating, optional or other rights and such qualifications, limitations or restrictions as provided in a resolution or resolutions adopted by our board of directors. Prior to the issuance of shares of a series of preferred stock, we are required by the General Corporation Law of the State of Delaware, or DGCL, to file a certificate of designation with the Secretary of State of the State of Delaware. The certificate of designation set forth, for each such series, the designations, powers, preferences, rights, qualifications, limitations and restrictions, established by the resolution or resolutions of our board of directors as described above.

Our board of directors, without stockholder approval, could issue one or more series of our preferred stock with voting, economic or other rights that are senior or superior to those of our common stock that could, among other things, dilute the voting power of our common stock, reduce the likelihood that holders of our common stock will receive dividend payments (if we were to elect to pay dividends) or payments in the event of our liquidation, dissolution or winding-up, and delay, deter or prevent a change in control or other takeover of our company.

Shareholder Rights Plan; Series A Participating Preferred Stock

Our board of directors has established a shareholder rights plan and, in connection therewith, has authorized the issuance of 100,000 shares of our Series A Participating Preferred Stock, or the Junior Preferred Stock. Both our shareholder rights plan and our authorized but unissued Junior Preferred Stock include terms and conditions which could discourage a takeover or other transaction that holders of some or a majority of common stock might believe to be in their best interests.

Pursuant to the Rights Agreement (as defined below), our board of directors has authorized the issuance of 136 preferred share purchase rights, or a Right , for each outstanding share of our common stock, including any shares offered pursuant to this prospectus and any applicable prospectus supplement. Each Right entitles its

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holder to purchase one one-thousandth of a share of our Junior Preferred Stock (we refer to this fractional share as an Unit) at a price of $15.00. As described below, this fraction of a share of Junior Preferred Stock is intended to give the owner approximately the same dividend, voting and liquidation rights as would one share of our common stock. However, prior to exercise, a Right does not give its owner any dividend, voting, liquidation or other rights as a stockholder.

The terms of the rights are set forth in a rights agreement dated as of May 13, 2005, as amended, by and between American Stock Transfer & Trust Company, LLC, as rights agent, and us, which is referred to herein as the Rights Agreement.

Subject to certain exceptions, upon the earlier to occur of (i) the close of business on the tenth day after a public announcement that a person, together with all affiliates or associates of such person, which we refer to as acquiring person, has acquired beneficial ownership of 15% or more of our outstanding common stock, subject to certain exceptions, or (ii) 10 business days (or such later date as may be determined by action of our board of directors prior to such time as any person becomes an acquiring person) following the commencement of a tender or exchange offer which would result in the beneficial ownership by an acquiring person of 15% or more of such outstanding common stock (the earlier of such dates is referred to as the distribution date), the Rights will be evidenced by our common stock certificates.

The Rights are currently evidenced by the certificates that represent our common stock and trade with, and are inseparable from, the underlying common stock. Until the distribution date (or earlier redemption or expiration of the Rights), the surrender for transfer of any certificates of our common stock will also constitute the transfer of the Rights associated with the common stock represented by such certificate. As soon as practicable following the distribution date, if any, separate certificates evidencing the Rights will be mailed to holders of record of our common stock as of the close of business on the distribution date and such separate Rights certificates alone will evidence the Rights.

The Rights are not exercisable until the distribution date. The Rights will expire at the close of business on May 13, 2015 unless that final expiration date is extended or unless the Rights are earlier redeemed or exchanged by us, in each case as described below.

The purchase price payable, and the number of Units of Junior Preferred Stock or other securities or property issuable, upon exercise of the Rights are subject to adjustment from time to time to prevent dilution (i) in the event of a stock dividend on, or a subdivision, combination or reclassification of, the Junior Preferred Stock, (ii) upon the grant to holders of the Units of Junior Preferred Stock of certain rights, options or warrants to subscribe for or purchase Units of Junior Preferred Stock (or shares having the same or more favorable rights, privileges and preferences as the Junior Preferred Stock, which we refer to as equivalent preferred stock) at a price, or securities convertible into Units of Junior Preferred Stock or equivalent preferred stock with a conversion price, less than the then current market price of the Units of Junior Preferred Stock, or (iii) upon the distribution to holders of the Units of Junior Preferred Stock of evidences of indebtedness, cash or assets (excluding regular periodic cash dividends paid out of earnings or retained earnings or dividends payable in Units of Junior Preferred Stock) or of subscription rights, options or warrants other than those referred to above.

The number of outstanding Rights and the number of Units of Junior Preferred Stock issuable upon exercise of each Right are also subject to adjustment in the event of a stock split of our common stock or a stock dividend on the common stock payable in common stock or subdivisions, consolidations or combinations of the common stock occurring, in any such case, prior to the distribution date.

The Junior Preferred Stock purchasable upon exercise of the Rights will not be redeemable. The Junior Preferred Stock will rank senior in right of payment to our common stock, and, unless otherwise provided with respect to a particular series of our preferred stock, junior in right of payment to our preferred stock, with respect to dividends and distributions in the event of our liquidation, dissolution and winding-up. Each share of Junior Preferred Stock will be entitled to a minimum quarterly payment of $10.00 per share, or, if greater, an aggregate

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dividend of one one-hundred thirty-sixth (1/136th) of 1,000 times the dividend (other than dividends payable in common stock) declared per share of our common stock. In the event of our liquidation, dissolution or winding-up, the holders of shares of our Junior Preferred Stock will be entitled to receive, for each share of Junior Preferred Stock and after payment of or provision for our debts and other liabilities and the preferential amounts, if any, to be distributed to holders of any other outstanding shares of our preferred stock, a minimum liquidation payment of $1,000 per share (plus any accrued but unpaid dividends), or, if greater, an aggregate payment of one one-hundred thirty-sixth (1/136th) of 1,000 times the payment made per share of our common stock. Each share of Junior Preferred Stock will have one one-hundred thirty-sixth (1/136th) of 1,000 votes on all matters submitted to a vote of our stockholders and shall vote together with the holders of our common stock as one class on all matters submitted to a vote of our stockholders. In the event of any merger, consolidation or other transaction in which shares of our common stock are exchanged, each share of Junior Preferred Stock will be exchanged or changed in an amount per share equal to one one-hundred thirty-sixth (1/136th) of 1,000 times the amount received per share of common stock. The foregoing rights are protected by customary anti-dilution provisions.

The foregoing dividend, liquidation and voting rights of the Junior Preferred Stock are intended to result in each Unit of Junior Preferred Stock purchasable upon exercise of a Right having a value that approximates the value of one share of common stock.

If, after the Rights become exercisable, we are acquired in a merger or other business combination transaction with an acquiring person or one of its affiliates, or 50% or more of our consolidated assets or earning power are sold to an acquiring person or one of its affiliates, the Rights Agreement requires that proper provision be made so that each holder of a Right will thereafter have the right to receive, upon exercise thereof at the then current exercise price of the Right, that number of shares of common stock of the acquiring person which at the time of such transaction will have a market value of two times the exercise price of the Right.

If any person or group of affiliated or associated persons becomes the beneficial owner of 15% or more of the outstanding shares of our common stock, the Rights Agreement requires, subject to certain exceptions, that proper provision be made so that each holder of a Right, other than Rights beneficially owned by the acquiring person (which will thereafter be unexercisable), will have the right to receive for a period of 60 days upon exercise that number of shares of our common stock or Units of Junior Preferred Stock (or cash, other securities or property) having a market value of two times the exercise price of the Right.

At any time after the acquisition by a person or group of affiliated or associated persons of beneficial ownership of 15% or more of the outstanding shares of our common stock, subject to certain exceptions, and prior to the acquisition by such person or group of 50% or more of the outstanding common stock, our board of directors may exchange the Rights (other than Rights owned by such person or group, which will have become void), in whole or in part, at an exchange ratio per Unit of Junior Preferred Stock equal to the purchase price per Unit of Junior Preferred Stock upon exercise of a Right divided by the then current market price per Unit of Junior Preferred Stock on the earlier of (i) the date on which any person becomes an acquiring person and (ii) the date on which a tender or exchange offer is announced which, if consummated would result in the offerer being the beneficial owner of 15% or more of the shares of our common stock then outstanding.

With certain exceptions, no adjustment to the purchase price will be required until cumulative adjustments require an adjustment of at least 1% in the purchase price. No fractional shares of Junior Preferred Stock will be issued (other than fractions which are integral multiples of one one-thousandth of a share of Junior Preferred Stock, which may, at our election, be evidenced by depositary receipts) and, in lieu thereof, an adjustment in cash will be made based on the market price of the Units of Junior Preferred Stock on the last trading day prior to the date of exercise.

At any time on or prior to the public announcement that there is an acquiring person, our board of directors may redeem the Rights in whole, but not in part, at a price of $0.0005 per Right. The redemption of the Rights may be made effective at such time, on such basis and with such conditions as our board of directors in its sole

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discretion may establish. Immediately upon any redemption of the Rights, the right to exercise the Rights will terminate and the only right of the holders of Rights will be to receive the redemption price. The Rights are also redeemable after public announcement that there is an acquiring person under certain circumstances as specified in the Rights Agreement.

Generally, the terms of the Rights and the Rights Agreement may be amended by our board of directors without the consent of the holders of the Rights except that from and after such time that there is an acquiring person no amendment may adversely affect the interests of the holders of the Rights. However, our board of directors may not amend the Rights Agreement to lower the threshold at which a person or group becomes an acquiring person to below 10% of our outstanding common stock. In addition, our board of directors may not cause a person or group to become an acquiring person by lowering this threshold below the percentage interest that such person or group already owns.

Until a Right is exercised, the holder of a Right will have no rights, by virtue of such holder s ownership of a Right, as our stockholder, including, without limitation, the right to vote or to receive dividends.

The Rights have certain anti-takeover effects. The Rights will cause substantial dilution to a person or group that attempts to acquire us on terms not approved by our board of directors, except pursuant to an offer conditioned on a substantial number of Rights being acquired. The Rights should not interfere with any merger or other business combination approved by our board of directors since the Rights may be redeemed by us at the redemption price prior to the occurrence of a distribution date. The foregoing description of the Rights, the Rights Agreement and the Junior Preferred Stock is not complete and is qualified in its entirety by reference to the Rights Agreement and our certificate of incorporation, as amended, which are incorporated by reference as exhibits to the registration statement of which this prospectus is a part and may be obtained as described under Where You Can Find More Information; Incorporation by Reference.

Anti-Takeover Effects of Delaware Law

We are subject to the provisions of Section 203 of the Delaware General Corporation Law. Under Section 203, we are generally prohibited, subject to certain exceptions, from engaging in any business combination with any interested stockholder (as those terms are defined in Section 203) for a period of three years following the time that this stockholder became an interested stockholder unless:

- prior to this time, our board of directors approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of our voting stock outstanding at the time the transaction commenced, excluding shares owned by persons who are our directors and also officers and by employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or
- at or subsequent to such time, the business combination is approved by our board of directors and authorized at an annual or special meeting of our stockholders, and not by written consent, by the affirmative vote of at least 66 2/3% of the outstanding voting stock that is not owned by the interested stockholder.

Under Section 203, a business combination includes in general, with respect to a Delaware corporation such as us:

any merger or consolidation involving the corporation and the interested stockholder;

any sale, transfer, pledge or other disposition to or with the interested stockholder of assets of the corporation with an aggregate market value equal to or greater than 10% of either the aggregate market value of the corporation s consolidated assets or the aggregate market value of the corporation s outstanding stock;

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any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder, subject to limited exceptions;

any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; or

the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder, in general and subject to exceptions, as (a) an entity or person beneficially owning, or within three years prior to the determination of interested stockholder status did own, 15% or more of the outstanding voting stock of the corporation and (b) any affiliate or associate (as those terms are defined in Section 203) of the corporation that was the owner of 15% or more of the outstanding voting stock of the corporation within the prior three years, and affiliates and associates of any of the foregoing persons.

The forgoing description of some of the terms of Section 203 of the Delaware General Corporation Law is not complete and is qualified by reference to Section 203.

Anti-Takeover Effects of Our Certificate of Incorporation and Bylaws

Certain provisions of our certificate of incorporation, as amended, and bylaws, as amended, as well as the provisions of our Rights Agreement and Section 203 of the Delaware General Corporation Law described above, could have the effect of delaying, deterring or preventing another party from acquiring or seeking to acquire control of us. These provisions are intended to discourage certain types of coercive takeover practices and inadequate takeover bids and to encourage anyone seeking to acquire control of us to negotiate first with our board of directors. However, these provisions may also delay, deter or prevent a change in control or other takeover of our company that our stockholders might consider to be in their best interests, including transactions that might result in a premium being paid over the market price of our common stock and also may limit the price that investors are willing to pay in the future for our common stock. These provisions may also have the effect of preventing changes in our management.

Our certificate of incorporation, as amended, and bylaws, as amended, include anti-takeover provisions that:

authorize our board of directors, without further action by the stockholders, to issue preferred stock in one or more series and, with respect to each series, to fix the number of shares constituting that series and to establish the rights and other terms of that series, which may include dividend and liquidation rights and preferences, conversion rights and voting rights;

provide that the number of directors that shall constitute our board of directors shall be fixed exclusively by resolutions adopted by our board of directors and that vacancies on our board of directors, including newly created directorships resulting from any increase in the number of our directors, shall, unless otherwise determined by our board of directors or required by law, be filled only by the affirmative vote of a majority of our directors then in office, even though less than a quorum, and not by our stockholders;

require that actions to be taken by our stockholders may only be taken at an annual or special meeting of our stockholders and not by written consent;

specify that special meetings of our stockholders can be called only by the Chairman of our board of directors, our Chief Executive Officer, our President or our board of directors and not by our stockholders or any other persons;

establish advance notice procedures for stockholders to submit nominations of candidates for election to our board of directors and other proposals to be brought before a stockholders meeting;

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require the affirmative vote of the holders of at least $66^{2}/_{3}\%$ of the voting power of all of our then-outstanding shares of capital stock entitled to vote generally at an election of directors in order to remove the board of directors or any individual director without cause;

provide that both our board of directors and our stockholders may adopt, amend or repeal our bylaws, provided that, in addition to any vote of any class or series of stock required by law or our certificate of incorporation, as amended, the affirmative vote of the holders of $66^{2}/_{3}\%$ of the voting power of all then-outstanding shares of our capital stock entitled to vote generally in the election of directors shall be required for our stockholders to adopt, amend or repeal any provision of our bylaws; and

do not give the holders of our common stock cumulative voting rights with respect to the election of directors, which means that the holders of a majority of our outstanding shares of common stock can elect all directors standing for election by the holders of our common stock.

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DESCRIPTION OF OTHER SECURITIES

We will set forth in the applicable prospectus supplement a description of any warrants to purchase common stock or preferred stock or units, which will consist of one or more shares of common stock or preferred stock and one or more warrants to purchase common stock or preferred stock, issued by us that may be offered and sold pursuant to this prospectus.

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GLOBAL SECURITIES

Book-Entry, Delivery and Form

Unless we indicate differently in a prospectus supplement, the securities initially will be issued in book-entry form and represented by one or more global notes or global securities, or, collectively, global securities. The global securities will be deposited with, or on behalf of, The Depository Trust Company, New York, New York, as depositary, or DTC, and registered in the name of Cede & Co., the nominee of DTC. Unless and until it is exchanged for individual certificates evidencing securities under the limited circumstances described below, a global security may not be transferred except as a whole by the depositary to its nominee or by the nominee to the depositary, or by the depositary or its nominee to a successor depositary or to a nominee of the successor depositary.

DTC has advised us that it is:

a limited-purpose trust company organized under the New York Banking Law;

a banking organization within the meaning of the New York Banking Law;

a member of the Federal Reserve System;

a clearing corporation within the meaning of the New York Uniform Commercial Code; and

a clearing agency registered pursuant to the provisions of Section 17A of the Exchange Act.

DTC holds securities that its participants deposit with DTC. DTC also facilitates the settlement among its participants of securities transactions, such as transfers and pledges, in deposited securities through electronic computerized book-entry changes in participants accounts, thereby eliminating the need for physical movement of securities certificates. Direct participants in DTC include securities brokers and dealers, including underwriters, banks, trust companies, clearing corporations and other organizations. DTC is a wholly-owned subsidiary of The Depository Trust & Clearing Corporation, or DTCC. DTCC is the holding company for DTC, National Securities Clearing Corporation and Fixed Income Clearing Corporation, all of which are registered clearing agencies. DTCC is owned by the users of its regulated subsidiaries. Access to the DTC system is also available to others, which we sometimes refer to as indirect participants, that clear through or maintain a custodial relationship with a direct participant, either directly or indirectly. The rules applicable to DTC and its participants are on file with the SEC.

Purchases of securities under the DTC system must be made by or through direct participants, which will receive a credit for the securities on DTC s records. The ownership interest of the actual purchaser of a security, which we sometimes refer to as a beneficial owner, is in turn recorded on the direct and indirect participants records. Beneficial owners of securities will not receive written confirmation from DTC of their purchases. However, beneficial owners are expected to receive written confirmations providing details of their transactions, as well as periodic statements of their holdings, from the direct or indirect participants through which they purchased securities. Transfers of ownership interests in global securities are to be accomplished by entries made on the books of participants acting on behalf of beneficial owners. Beneficial owners will not receive certificates representing their ownership interests in the global

securities, except under the limited circumstances described below.

To facilitate subsequent transfers, all global securities deposited by direct participants with DTC will be registered in the name of DTC s partnership nominee, Cede & Co., or such other name as may be requested by an authorized representative of DTC. The deposit of securities with DTC and their registration in the name of Cede & Co. or such other nominee will not change the beneficial ownership of the securities. DTC has no knowledge of the actual beneficial owners of the securities. DTC s records reflect only the identity of the direct participants to whose accounts the securities are credited, which may or may not be the beneficial owners. The participants are responsible for keeping account of their holdings on behalf of their customers.

So long as the securities are in book-entry form, you will receive payments and may transfer securities only through the facilities of the depositary and its direct and indirect participants. We will maintain an office or agency in the location specified in the prospectus supplement for the applicable securities, where notices and demands in respect of the securities and the indenture may be delivered to us and where certificated securities may be surrendered for payment, registration of transfer or exchange.

Conveyance of notices and other communications by DTC to direct participants, by direct participants to indirect participants and by direct participants and indirect participants to beneficial owners will be governed by arrangements among them, subject to any legal requirements in effect from time to time.

Redemption notices will be sent to DTC. If less than all of the securities of a particular series are being redeemed, DTC s practice is to determine by lot the amount of the interest of each direct participant in the securities of such series to be redeemed.

Neither DTC nor Cede & Co. (or such other DTC nominee) will consent or vote with respect to the securities. Under its usual procedures, DTC will mail an omnibus proxy to us as soon as possible after the record date. The omnibus proxy assigns the consenting or voting rights of Cede & Co. to those direct participants to whose accounts the securities of such series are credited on the record date, identified in a listing attached to the omnibus proxy.

So long as securities are in book-entry form, we will make payments on those securities to the depositary or its nominee, as the registered owner of such securities, by wire transfer of immediately available funds. If securities are issued in definitive certificated form under the limited circumstances described below, we will have the option of making payments by check mailed to the addresses of the persons entitled to payment or by wire transfer to bank accounts in the United States designated in writing to the applicable trustee or other designated party at least 15 days before the applicable payment date by the persons entitled to payment, unless a shorter period is satisfactory to the applicable trustee or other designated party.

Redemption proceeds, distributions and dividend payments on the securities will be made to Cede & Co., or such other nominee as may be requested by an authorized representative of DTC. DTC s practice is to credit direct participants accounts upon DTC s receipt of funds and corresponding detail information from us on the payment date in accordance with their respective holdings shown on DTC records. Payments by participants to beneficial owners will be governed by standing instructions and customary practices, as is the case with securities held for the account of customers in bearer form or registered in street name. Those payments will be the responsibility of participants and not of DTC or us, subject to any statutory or regulatory requirements in effect from time to time. Payment of redemption proceeds, distributions and dividend payments to Cede & Co., or such other nominee as may be requested by an authorized representative of DTC, is our responsibility, disbursement of payments to direct participants is the responsibility of DTC, and disbursement of payments to the beneficial owners is the responsibility of direct and indirect participants.

Except under the limited circumstances described below, purchasers of securities will not be entitled to have securities registered in their names and will not receive physical delivery of securities. Accordingly, each beneficial owner must rely on the procedures of DTC and its participants to exercise any rights under the securities and the indenture.

The laws of some jurisdictions may require that some purchasers of securities take physical delivery of securities in definitive form. Those laws may impair the ability to transfer or pledge beneficial interests in securities.

DTC may discontinue providing its services as securities depositary with respect to the securities at any time by giving reasonable notice to us. Under such circumstances, in the event that a successor depositary is not obtained,

securities certificates are required to be printed and delivered.

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As noted above, beneficial owners of a particular series of securities generally will not receive certificates representing their ownership interests in those securities. However, if:

- DTC notifies us that it is unwilling or unable to continue as a depositary for the global security or securities representing such series of securities or if DTC ceases to be a clearing agency registered under the Exchange Act at a time when it is required to be registered and a successor depositary is not appointed within 90 days of the notification to us or of our becoming aware of DTC s ceasing to be so registered, as the case may be;

- we determine, in our sole discretion, not to have such securities represented by one or more global securities; or

- an Event of Default has occurred and is continuing with respect to such series of securities,

we will prepare and deliver certificates for such securities in exchange for beneficial interests in the global securities. Any beneficial interest in a global security that is exchangeable under the circumstances described in the preceding sentence will be exchangeable for securities in definitive certificated form registered in the names that the depositary directs. It is expected that these directions will be based upon directions received by the depositary from its participants with respect to ownership of beneficial interests in the global securities.

We have obtained the information in this section and elsewhere in this prospectus concerning DTC and DTC s book-entry system from sources that are believed to be reliable, but we take no responsibility for the accuracy of this information.

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PLAN OF DISTRIBUTION

We may sell the offered securities from time to time:

through underwriters or dealers;

through agents;

directly to one or more purchasers; or

through a combination of any of these methods of sale.

We will identify the specific plan of distribution, including any underwriters, dealers, agents or direct purchasers and their compensation in the applicable prospectus supplement.

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LEGAL MATTERS

Latham & Watkins LLP will pass upon certain legal matters relating to the issuance and sale of the securities offered hereby on behalf of Raptor Pharmaceutical Corp. Additional legal matters may be passed upon for us or any underwriters, dealers or agents, by counsel that we will name in the applicable prospectus supplement.

EXPERTS

The consolidated balance sheets as of December 31, 2013 and 2012, and the related consolidated statements of operations and comprehensive loss, stockholders equity (deficit) and cash flows for the year ended December 31, 2013 and for the four month period ended December 31, 2012, the financial statement schedule, and management s assessment of the effectiveness of internal control over financial reporting, that are incorporated by reference in this prospectus and elsewhere in the registration statement have been so incorporated by reference in reliance upon the reports of Grant Thornton LLP, independent registered public accountants, upon the authority of said firm as experts in accounting and auditing. The consolidated statements of operations and comprehensive loss, stockholders equity (deficit) and cash flows for the fiscal years ended August 31, 2012 and 2011, the financial statement schedule, and management s assessment of the effectiveness of internal control over financial reporting, that are incorporated by reference in this prospectus and elsewhere in the registration statement have been so incorporated by reference in reliance upon the reports of Burr Pilger Mayer, Inc., independent registered public accountants, upon the authority of said firm as experts in accounting and auditing.

With respect to the unaudited interim financial information for the quarters ended March 31, 2013, June 30, 2013 and September 30, 2013, incorporated by reference in this prospectus and elsewhere in the registration statement, Grant Thornton LLP has reported that they have applied limited procedures in accordance with professional standards for a review of such information. However, their separate reports thereon state that they did not audit and they do not express an opinion on that interim financial information. Accordingly, the degree of reliance on their report on such information should be restricted in light of the limited nature of the review procedures applied. In addition, Grant Thornton LLP is not subject to the liability provisions of Section 11 of the Securities Act of 1933 for their report on the unaudited interim financial information because that report is not a report or a part of the registration statement prepared or certified by the accountants within the meaning of the Sections 7 and 11 of that Act.

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$46,193,473.43

Raptor Pharmaceutical Corp.

Common Stock

Prospectus Supplement

August 21, 2014

Cowen and Company