PROGENICS PHARMACEUTICALS INC
Form 424B5
February 21, 2014
Table of Contents

Filed pursuant to Rule 424(b)(5)
Registration Statement No. 333-193521

PROSPECTUS SUPPLEMENT

(to Prospectus dated February 5, 2014)

7,608,696 Shares

Progenics Pharmaceuticals, Inc.

Common Stock

We are offering 7,608,696 shares of our common stock. Our common stock is quoted on The NASDAQ Global Select Market under the symbol PGNX. On February 20, 2014, the last reported sale price of our common stock on The NASDAQ Global Select Market was $4.90 per share.

Investing in our common stock involves a high degree of risk. Please read Risk Factors beginning on page S-4 of this prospectus supplement and in the documents incorporated by reference in this prospectus supplement.

Neither the U.S. 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.

	PER SHARE	TOTAL
Public Offering Price	$ 4.600	$ 35,000,001.60
Underwriting Discounts and Commissions	0.276	2,100,000.10
Proceeds to Progenics Pharmaceuticals, Inc. before expenses	4.324	32,900,001.50

Delivery of the shares of common stock is expected to be made on or about February 26, 2014. We have granted the underwriters an option for a period of 30 days to purchase up to an additional 1,141,304 shares of our common stock. If the underwriters exercise the option in full, the total underwriting discounts and commissions payable by us will be $2,415,000.00, and the total proceeds to us, before expenses, will be $37,835,000.00.

Sole Book-Running Manager

Jefferies

Needham & Company **Brean Capital**

Prospectus Supplement dated February 21, 2014

Table of Contents

TABLE OF CONTENTS

Table of Contents

You should rely only on the information contained in or incorporated by reference in this prospectus supplement, the accompanying prospectus and in any free writing prospectus that we have authorized for use in connection with this offering. We have not, and the underwriters have not, authorized anyone to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We are not, and the underwriters are not, making 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 supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering is accurate only as of the date of the respective document in which the information appears. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering in their entirety before making an investment decision.

For investors outside the United States: Neither we nor the underwriters have done anything that would permit this offering or possession or distribution of this prospectus supplement and the accompanying prospectus in any jurisdiction where action for that purpose is required, other than the United States. You are required to inform yourselves about and to observe any restrictions relating to this offering and the distribution of this prospectus supplement and the accompanying prospectus outside of the United States.

Table of Contents

ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus are part of a registration statement on Form S-3 that we filed with the U.S. Securities and Exchange Commission (SEC) under the Securities Act of 1933, as amended (Securities Act), on January 23, 2014, and was declared effective by the SEC on February 5, 2014 (Registration Statement).

This document is in two parts. The first part is this prospectus supplement, which describes the terms of this offering of common stock and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference in this prospectus supplement and the accompanying prospectus. The second part, the accompanying prospectus contained in the Registration Statement, including the documents incorporated by reference therein, provides more general information, some of which may not apply to this offering. Generally, when we refer to this prospectus supplement or prospectus, we are referring to both parts of this document combined. To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in the accompanying prospectus or in any document incorporated by reference that was filed with the SEC before the date of this prospectus supplement, on the other hand, you should rely on the information in this prospectus supplement. If any statement in one of these documents is inconsistent with a statement in another document having a later date for example, a document incorporated by reference in the accompanying prospectus the statement in the document having the later date modifies or supersedes the earlier statement.

This prospectus supplement and the accompanying prospectus contain and incorporate by reference market data, industry statistics and other data that have been obtained or compiled from information made available by third parties. These data, to the extent they contain estimates or projections, involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates or projections. Industry publications and other reports we have obtained from independent parties generally state that the data contained in these publications or other reports have been obtained in good faith or from sources considered to be reliable, but they do not guarantee the accuracy or completeness of such data.

All references in this prospectus supplement and the accompanying prospectus to Progenics, PGNX, the Company, we, us, our or similar references refer to Progenics Pharmaceuticals, Inc., a Delaware corporation, and its subsidiaries, except where the context otherwise requires or as otherwise indicated.

This prospectus supplement, the accompanying prospectus and the information incorporated herein and therein by reference, include trademarks, service marks and trade names owned by us or other companies. All trademarks, service marks and trade names included or incorporated by reference in this prospectus supplement or the accompanying prospectus are the property of their respective owners.

You should read this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering in their entirety before making an investment decision. You should also read and consider the information in the documents to which we have referred you in the sections of this prospectus supplement entitled Where You Can Find More Information and Incorporation of Certain Information by Reference, and in particular the periodic and current reporting documents we file with the SEC.

Table of Contents

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights certain information about us, this offering and selected information contained elsewhere in or incorporated by reference in this prospectus supplement and the accompanying prospectus. This summary is not complete and does not contain all of the information that you should consider before deciding whether to invest in our common stock. For a more complete understanding of our company and this offering, we encourage you to read and consider carefully the more detailed information in this prospectus supplement and the accompanying prospectus, including the information incorporated by reference in this prospectus supplement and the accompanying prospectus, and the information included in any free writing prospectus that we have authorized for use in connection with this offering, including the information referred to under the heading Risk Factors in this prospectus supplement beginning on page S-4.

Overview

Progenics develops innovative medicines for oncology. A significant part of our research and development efforts centers on prostate specific membrane antigen (PSMA), a protein found at high levels on the surface of prostate cancer cells and also on the neovasculature of a number of other types of solid tumors. We are conducting phase 2 clinical trials of two product candidates for prostate cancer targeted toward PSMA: our therapeutic candidate, PSMA ADC, a fully human monoclonal antibody-drug conjugate (ADC), and MIP-1404, an imaging agent candidate in development by our Molecular Insight Pharmaceuticals, Inc. subsidiary. We are also developing Azedra , an ultra-orphan radiotherapy candidate in a pivotal phase 2 clinical trial for pheochromocytoma, for which we now plan to continue patient recruitment after making drug supply manufacturing arrangements. Among other assets in our pipeline of targeted radiotherapy and molecular imaging compounds are a group of small molecule therapeutics, MIP-1095, -1555 and -1558, in preclinical study for metastatic prostate cancer and other PSMA-expressing cancers.

Our acquisition of Molecular Insight in January 2013, which expanded our portfolio of late-stage oncology candidates, included the issuance of approximately 4.6 million Progenics shares in a private transaction not taxable to us. Under the acquisition agreement, we are obligated to pay potential future milestone payments, in cash or Progenics stock at our option, of up to $23.0 million contingent upon achievement of specified commercialization events and $70.0 million upon achieving sales targets relating to the products of Molecular Insight in development at the time of the acquisition. Approximately 94,000 shares from an original 500,000 share escrow, which expires in April 2014, have been returned to Progenics to date pursuant to the agreement s adjustment provisions.

We have developed internally and acquired from research institutions, pharmaceutical and biotechnology companies certain compounds and technologies which we are advancing with other parties, including our first commercial drug, Relistor® (methylnaltrexone bromide) subcutaneous injection for the treatment of opioid induced constipation (OIC), which we have licensed to Salix Pharmaceuticals, Inc. worldwide other than Japan, where we have licensed the subcutaneous formulation of the drug to Ono Pharmaceutical Co., Ltd., and two internally-developed properties which we transitioned in 2012 to MedImmune, LLC and CytoDyn Inc., respectively. We continue to consider opportunities for strategic collaborations, out-licenses and other arrangements with biopharmaceutical companies involving our proprietary research, development and clinical programs, and may in the future also in-license or acquire additional oncology compounds and/or programs.

Our current principal sources of revenue from operations are royalty, commercialization milestone and revenue-sharing payments from Salix s Relistor operations. Royalty and milestone payments from Relistor depend on success in development and commercialization, which is dependent on many factors, such as the actions of Salix and Ono, decisions by the U.S. Food and Drug Administration (FDA) and other regulatory bodies, the outcome of clinical and other testing of Relistor, and, to the extent requested by our collaboration partners, our own efforts. We and Salix

have sought to expand the availability of subcutaneous Relistor to patients taking opioids for non-cancer pain and who suffer from OIC as a result, and to develop an oral formulation of

Table of Contents

methylnaltrexone for use by such patients. In July 2012, the FDA issued a Complete Response Letter for the supplemental New Drug Application (sNDA) for Relistor injection for subcutaneous use for the treatment of OIC in adult patients with chronic, non-cancer pain, in which the FDA requested additional clinical data. After an End-of-Review meeting in October 2012, the FDA s Division of Gastroenterology and Inborn Errors Products expressed a concern that there may be a risk associated with the chronic use of mu-opioid receptor antagonists in patients who are taking opioids for chronic pain, and, in order to understand this potential risk, the Division communicated that a very large, well-controlled, chronic administration trial will have to be conducted to assess the safety of any mu-opioid receptor antagonist prior to market approval for the treatment of patients with OIC who are taking opioids for chronic, non-cancer pain. Salix subsequently held discussions with the Division and expressed the view that the post-marketing, clinical and preclinical data currently available for Relistor adequately demonstrate an appropriate and expected safety profile sufficient to permit the approval of the current Relistor sNDA. In response to Salix s formal appeal of the FDA s Complete Response Letter, the FDA informed Salix and us in June 2013 that it will seek input from an Anesthetic and Analgesic Drug Products Advisory Committee (AADPAC). The FDA recently informed Salix and us that the proposed meeting of AADPAC will convene in the near future. The FDA has also stated that it will take action under the appeal within 30 days after receiving input from AADPAC.

At the time Salix and Progenics announced the FDA s determination to convene the AADPAC, we expressed our belief that some of the areas being considered for discussion during the meeting would include the potential for drugs in Relistor s class to cause withdrawal symptoms; the strength of a potential cardiovascular signal seen with another drug in this class of drugs and the available safety data with Relistor in regards to a potential cardiovascular signal; and the need and timing (pre-approval vs. post-approval) of major adverse cardiac events studies with drugs of this class. We also announced that the FDA had communicated that it was convening the AADPAC for the following reasons:

- The potential cardiovascular safety signal observed in the 12-month safety trial of another peripheral mu-opioid antagonist for the treatment of opioid-induced constipation in patients with chronic non-cancer pain raises concern for this class of drug products.

- The Relistor supplemental application contains only uncontrolled long-term safety data, and while there is no cardiovascular signal apparent in this data, the lack of a control population does not allow a definitive evaluation to be made to rule out a potential cardiovascular safety signal.

- FDA needs to provide consistent advice regarding the need for Major Adverse Cardiovascular Event studies to applicants developing drug products in this class for this indication. For this reason, a broader discussion of the potential for cardiovascular events across the drug class is necessary.

With regard to our license to Ono of subcutaneous Relistor for development in Japan, we commenced an arbitration in October 2013 under the provisions of our license agreement following a communication from Ono that it has determined to discontinue development of subcutaneous Relistor in Japan because of commercial concerns that Ono contends would permit it to cease development and terminate the agreement. Under the agreement, Ono may cease development of subcutaneous Relistor only if it terminates the agreement, which it may do unilaterally only if Progenics is in material default. Ono has neither asserted that Progenics is in material default nor terminated the agreement.

Corporate Information

Progenics was incorporated in Delaware in 1986. We maintain our executive offices at 777 Old Saw Mill River Road, Tarrytown, New York 10591, and our main telephone number is (914) 789-2800. We maintain a website at www.progenics.com, which contains information about Progenics, Molecular Insight and our other subsidiaries. The information contained in, or that can be accessed through, our website is not part of, and is not incorporated into, this prospectus supplement or the accompanying prospectus and should not be considered part of these documents.

Table of Contents

THE OFFERING

Common stock we are offering	**7,608,696 shares**
Common stock to be outstanding after this offering	**68,434,100 shares**

Option to Purchase Additional Shares

We have granted the underwriters an option to purchase 1,141,304 additional shares of our common stock. This option is exercisable, in whole or in part, for a period of 30 days from the date of this prospectus supplement.

Use of Proceeds

We intend to use the net proceeds from this offering for research and development and general corporate purposes. We may also use a portion of the net proceeds to acquire, license or invest in businesses, products product candidates, technologies, intellectual property or other assets that are complementary to our own. We regularly consider such opportunities, but have no current understandings, agreements or commitments to effect any such transaction. Pending the application of the net proceeds, we may invest the net proceeds in short-term, interest-bearing instruments or other investment-grade securities, certificates of deposits or short-term U.S. government securities. See Use of Proceeds on page S-22 of this prospectus supplement.

NASDAQ Global Select Market Listing

Our common stock is listed on The NASDAQ Global Select Market under the symbol PGNX.

Risk Factors

Investing in our common stock involves a high degree of risk. See Risk Factors beginning on page S-4 of this prospectus supplement.

Outstanding Shares

The number of shares of our common stock to be outstanding immediately after this offering is based on 60,825,404 shares outstanding as of September 30, 2013, and excludes as of such date:

- 5,458,254 shares of our common stock issuable upon the exercise of outstanding options, at a weighted average exercise price of $10.82 per share; and
- 3,538,114 shares of our common stock available for future issuance pursuant to our existing stock incentive plans.

Except as otherwise indicated, all information in the prospectus supplement assumes no exercise by the underwriters of their option to purchase additional shares.

Table of Contents

RISK FACTORS

An investment in our common stock involves a high degree of risk. Before deciding whether to invest in our common stock, you should consider carefully the risks discussed below, together with other information in this prospectus supplement, the accompanying prospectus, the information and documents incorporated by reference and in any free writing prospectus that we have authorized for use in connection with this offering. The risks described below may not be the only ones relating to our company, business or common stock or to this offering. Additional risks that we currently believe are immaterial may also impair our business operations. Our business, results of operation, financial condition, cash flow and prospects and the trading price of our common stock could be harmed as a result of any of these risks, and investors may lose all or part of their investment.

Risks of Our Business

The future of our business and operations depends on the success of our Relistor collaborations and our oncology research and development programs, including the programs and product candidates of our Molecular Insight subsidiary.

Our business and operations entail a variety of serious risks and uncertainties and are inherently risky. The research and development programs on which we focus, including those of Molecular Insight, which we acquired in January 2013, involve novel approaches to human therapeutics. Our product candidates are in pre-clinical or clinical development, and in some respects involve technologies with which we have limited prior experience. We are subject to the risks of failure inherent in the development of product candidates based on new technologies. There is little precedent for the successful commercialization of products based on our technologies, and there are a number of technological challenges that we must overcome to complete most of our development efforts. We may not be able successfully to develop further any of our product candidates. We and our Relistor and other collaborators must successfully complete clinical trials and obtain regulatory approvals for potential commercial products. Once approved, if at all, commercial product sales are subject to general and industry-specific local and international economic pressures such as those experienced worldwide over the recent past. With our strategy to focus on oncology research and development, these risks continue to be significant and may increase to the extent the oncology space becomes more competitive or less favored in the commercial marketplace.

Our integration of Molecular Insight has required significant efforts, including coordination of research and development, as well as finance, accounting, and information technology and other functions, all of which involve expense and significant management time. The success of this acquisition will depend on, among other things, the strength of the product candidates of Molecular Insight and their underlying technologies; results of clinical trials, regulatory applications and approvals; and our ability to fund or otherwise develop acquired candidates and programs, achieve available cost savings, efficiencies and synergies, and attract and retain employees and consultants with expertise and experience appropriate to these efforts. In addition, the estimated fair values of the assets and liabilities acquired in the acquisition of Molecular Insight reflected in our financial statements do not, given the uniqueness of and uncertainties attendant to those assets and liabilities, reflect actual transactions or quoted prices and may not correlate to any future values or results. Such information should not be interpreted or relied upon as indicative of any future value or results. Our failure to manage successfully any of the product candidates, technologies or programs of Molecular Insight could have an adverse impact on our business, and on the price of our stock.

We are dependent on Salix, Ono and other business partners to develop and commercialize Relistor, exposing us to significant risks.

We rely on Salix to complete development and obtain regulatory approvals for additional formulations of and indications for Relistor and, in the Japanese market, we rely on Ono to conduct clinical trials and obtain regulatory approvals. We are and will be dependent upon Salix, Ono and any other business partners with which we may collaborate in the future to perform and fund development, including clinical testing, of Relistor, make related regulatory filings and manufacture and market products, including for new indications and in new formulations, in their respective territories. Revenue from the sale of Relistor outside of Japan depends entirely upon the efforts of Salix and its sublicensees, which have significant discretion in determining the efforts and resources they apply to sales of Relistor. Ono will have similar discretion with respect to sales in Japan. Neither may be effective in

Table of Contents

obtaining approvals for new indications or formulations, marketing existing or future products or arranging for necessary sublicense or distribution relationships. Our business relationships with Salix, Ono and other partners may not be scientifically, clinically or commercially successful. For example, Salix has a variety of marketed products. Salix is not, however, a large diversified pharmaceutical company and does not have resources commensurate with such companies. Salix has its own corporate objectives, which may not be consistent with our best interests, and may change its strategic focus or pursue alternative technologies in a manner that results in reduced or delayed revenue to us. Changes of this nature might also occur if Salix were acquired or if its management changed.

Both Salix and Ono have significantly greater financial and managerial resources than we do, which either could draw upon in the event of a dispute. In October 2013, we commenced an arbitration with Ono under the provisions of our license agreement with Ono for development and commercialization of subcutaneous Relistor in Japan, following a communication from Ono that it has determined to discontinue development because of commercial concerns that Ono contends would permit it to cease development and terminate the license agreement. Ono s discontinuation of development and/or protracted dispute resolution proceedings could result in reduced or delayed, or in the elimination of, milestone and/or royalty revenue from subcutaneous Relistor development in Japan. Under our license agreement with Salix, in the event our license agreement with Ono terminates or rights thereunder otherwise revert to Progenics, our license agreement with Salix will extend to the license grants, territory and other rights provided in the license agreement with Ono automatically and without payment by Salix, as a result of which Salix and not Progenics would receive such rights. Disagreements, such as this current dispute with Ono, could lead to lengthy and expensive litigation or other dispute-resolution proceedings as well as extensive financial and operational consequences to us and have a material adverse effect on our business, results of operations and financial condition. In addition, independent actions may be taken by Salix and/or Ono concerning product development, marketing strategies, manufacturing and supply issues, and rights relating to intellectual property, including, as discussed below, Relistor s path forward in light of the July 2012 Complete Response Letter from the FDA.

As a result of the FDA s Complete Response Letter on Relistor for chronic pain, the Relistor program may be discontinued or otherwise at risk.

The FDA in July 2012 issued a Complete Response Letter in response to Salix s supplemental New Drug Application for Relistor for the treatment of OIC in adult patients with chronic, non-cancer pain. This development may result in Salix and/or Ono taking independent actions concerning product development, marketing strategies or other matters for Relistor, including termination of their efforts to develop and commercialize the drug. At an End-of-Review meeting in October 2012, the FDA s Division of Gastroenterology and Inborn Errors Products expressed a concern that there may be a risk associated with the chronic use of mu-opioid receptor antagonists in patients who are taking opioids for chronic pain, and, in order to understand this potential risk, the Division communicated that a very large, well-controlled, chronic administration trial will have to be conducted to assess the safety of any mu-opioid receptor antagonist prior to market approval for the treatment of patients with OIC who are taking opioids for chronic, non-cancer pain. In addition, the FDA informed Salix and Progenics in June 2013 that it will seek input from the Anesthetic and Analgesic Drug Products Advisory Committee (AADPAC), which is expected to convene in the near future. At the time Salix and Progenics announced the FDA s determination to convene the AADPAC, we expressed our belief that some of the areas being considered for discussion during the meeting would include the potential for drugs in Relistor s class to cause withdrawal symptoms; the strength of a potential cardiovascular signal seen with another drug in this class of drugs and the available safety data with Relistor in regards to a potential cardiovascular (CV) signal; and the need and timing (pre-approval vs. post-approval) of major adverse cardiac events (MACE) studies with drugs of this class.

Salix has disclosed in regulatory filings that it might terminate its development program for Relistor subcutaneous injection for treatment of OIC in chronic, non-cancer pain patients, and that additional information and additional

guidance from the FDA could result in the termination of its oral OIC Relistor development program. As noted in our risk factor on regulatory approvals below, if clinical trials indicate, or regulatory bodies are concerned about, actual or possible serious problems with the safety or efficacy of a product candidate, such as the concerns expressed in the FDA s Complete Response Letter and as described above, we or our collaborators may stop or significantly slow development or commercialization of affected products. As a result of such concerns, the development programs for subcutaneous and/or oral Relistor for chronic, non-cancer pain patients may be significantly delayed or terminated altogether. In such an event, we could be faced with either further developing and commercializing the drug on our

Table of Contents

own or with one or more substitute collaborators, either of which paths would subject us to the development, commercialization, collaboration and/or financing risks discussed in these risk factors. Any such significant action adverse to development and commercialization of Relistor could have a material adverse impact on our business, and on the price of our stock.

We are subject to extensive regulation, which can be costly and time consuming, may not lead to marketing approval for our product candidates, and can subject us to unanticipated limitations, restrictions, delays and fines.

Our business, products and product candidates are subject to comprehensive regulation by the FDA and comparable authorities in other countries. These agencies and other entities regulate the pre-clinical and clinical testing, safety, effectiveness, approval, manufacture, labeling, marketing, export, storage, recordkeeping, advertising, promotion and other aspects of our products and product candidates. We cannot guarantee that approvals of product candidates, processes or facilities will be granted on a timely basis, or at all. If we experience delays or failures in obtaining approvals, commercialization of our product candidates will be slowed or stopped.

For example, in clinical studies of one of our principal product candidates, PSMA ADC, investigators have reported serious adverse events (SAEs), including three deaths, in a small proportion of patients treated with the drug. Based on data currently available to us, the Company is continuing development of PSMA ADC and has not determined what effects, if any, treatment-related SAEs reported to date or that may be reported in the future may have on the development of PSMA ADC going forward. If, however, we, together with or independently of investigators participating in our clinical trials, or regulators evaluating PSMA ADC were to determine that this candidate cannot safely be administered to patients with sufficient therapeutic effect, we may determine to attempt to reformulate or otherwise change the candidate and/or its administration to alleviate such concerns, which could result in costs and delays that could impair the value of the candidate. If such costs and delays were sufficiently large, we could determine to abandon the PSMA ADC program. Concerns about the safety and/or efficacy of PSMA ADC could also make it more difficult or impossible for us to enter into licensing, collaboration or other arrangements with third parties for further development and commercialization of PSMA ADC. Any of these possibilities could have material adverse effects on Progenics business, its financial condition, and/or the price of our stock.

Even if we obtain regulatory approval for a product candidate, the approval may include significant limitations on indicated uses for which the product could be marketed or other significant marketing restrictions, such as a Risk Evaluation and Mitigation Strategy (REMS). For example, Relistor is only approved for OIC in patients with advanced illness and not for chronic, non-cancer pain, and our product candidates, if approved at all, may be subject to those or other such limitations and restrictions.

If we or our collaborators violate regulatory requirements at any stage, whether before or after marketing approval is obtained, we or they may be subject to forced removal of a product from the market, product seizure, civil and criminal penalties and other adverse consequences. Under our license agreement with Salix, we are dependent on Salix for compliance with these regulatory requirements as they apply to Relistor. Salix has disclosed that in February 2013 it received a subpoena from the U.S. Attorney s Office for the Southern District of New York requesting documents regarding its sales and promotional practices for Relistor and certain of its other products, that it is in the process of responding to the subpoena and intends to cooperate fully with the subpoena and related government investigation, that at the time of its disclosure it cannot predict or determine the timing or outcome of the inquiry or its impact on Salix s financial condition or results of operations, and that the laws and regulations regarding off-label promotion and the authorities interpretation of them might increase its expenses, impair its ability to effectively market its products, and limit its revenue.

Our products may face regulatory, legal or commercial challenges even after approval.

Even if a product receives regulatory approval:

- It might not obtain labeling claims necessary to make the product commercially viable (in general, labeling claims define the medical conditions for which a drug product may be marketed, and are therefore very important to the commercial success of a product), or may be required to carry Boxed or other warnings that adversely affect its commercial success.

- Approval may be limited to uses of the product for treatment or prevention of diseases or conditions that are relatively less financially advantageous to us than approval of greater or different scope or subject to an FDA-imposed REMS that imposes limits on the distribution or use of the product.

Table of Contents

- Side effects (including different or aggravated effects such as SAEs encountered in our PSMA ADC program) identified after the product is on the market might hurt sales or result in mandatory safety labeling changes, additional pre-clinical testing or clinical trials, imposition of a REMS, product recalls or withdrawals from the market.

- Efficacy or safety concerns (including those arising from SAEs heretofore or hereafter encountered in our PSMA ADC program) regarding a marketed product, or manufacturing or other problems, may lead to a recall, withdrawal of marketing approval, reformulation of the product, additional pre-clinical testing or clinical trials, changes in labeling, imposition of a REMS, the need for additional marketing applications, declining sales or other adverse events. These potential consequences may occur whether or not the concerns originate from subsequent testing or other activities by us, governmental regulators, other entities or organizations or otherwise, and whether or not they are scientifically justified. If products lose previously received marketing and other approvals, our business, results of operations and financial condition would be materially adversely affected.

We or our collaborators will be subject to ongoing FDA obligations and continuous regulatory review, and might be required to undertake post-marketing trials to verify the product s efficacy or safety or other regulatory obligations.

Competing products in development may adversely affect acceptance of our products.

We are aware of a number of products and product candidates, including ENTEREG® (alvimopan), AMITIZA® (lubiprostone), naloxegol, TD-1211 (in a phase 2 clinical testing by Theravance, Inc.) and TARGIN® (oxycodone/naloxone), which compete or may potentially compete with Relistor. Any of these approved products or product candidates, or others which may be developed in the future may achieve a significant competitive advantage relative to Relistor, and, in any event, the existing or future marketing and sales capabilities of these competitors may impair Salix s and/or Ono s ability to compete effectively in the market.

We are also aware of competitors, including Cubist Pharmaceuticals, Inc., Sucampo Pharmaceuticals, Inc. (in collaboration with Takeda Pharmaceutical Company Limited), AstraZeneca AB (in collaboration with Nektar Therapeutics), Theravance, Inc., Mundipharma International Limited, Janssen Biotech, Inc., Medivation, Inc., Algeta ASA, Jazz Pharmaceuticals Public Limited Company, MedImmune/Auven Therapeutics Spirogen, and academic and government institutions, which are developing alternative treatments for disease targets to which our research and development programs are directed, any of which or others which may be developed in the future may achieve a significant competitive advantage relative to any product we may develop.

Developing product candidates will require us to obtain additional financing. Our access to capital funding is uncertain.

We expect to continue to incur significant development expenditures for our product candidates. We do not have committed external sources of funding for most of these projects. Our expenditures will be funded from cash on hand, or we may seek additional external funding for them, most likely through collaborative, license or royalty financing agreements with one or more pharmaceutical companies, equity securities issuances, debt financings, or government grants or contracts. To the extent we raise additional capital by issuing equity securities in the future, including any sale and issuance of shares of common stock by us, from time to time, in at-the-market offerings under the Controlled Equity Offering℠ Sales Agreement we entered with Cantor Fitzgerald & Co. on January 23, 2014, existing stockholders could experience substantial dilution. New investors could have rights superior to existing stockholders, if securities other than common stock were to be issued. Any debt financing that we are able to obtain may involve operating covenants that restrict our business and significant repayment obligations. To the extent that we raise

additional funds through any new collaboration and licensing arrangements, we may be required to relinquish some rights to our technologies or product candidates, or grant licenses on terms that are not favorable to us.

We cannot predict when we will need additional funds, how much we will need, the form any financing may take or whether additional funds will be available at all, especially in light of current conditions in global credit and financial markets. Our need for future funding will depend on numerous factors, such as the availability of new product development projects; the achievement of events identified in our collaboration agreements that trigger payments to us from our collaboration partners, most of which are out of our control and rely entirely on the efforts of our partners; the progress and success of clinical trials and pre-clinical activities (including studies and manufacture

Table of Contents

of materials) of our product candidates conducted by our collaborators or us; the progress of research programs carried out by us; any changes in the breadth of our research and development programs; the progress of the research and development efforts of our collaborators; our ability to acquire or license other technologies or compounds that we seek to pursue; competing technological and market developments; the costs and timing of obtaining, enforcing and defending our patent and intellectual property rights; the costs and timing of regulatory approvals and filings by us and our collaborators; our ability to manage our growth; and any unforeseen litigation. These factors may be more important with respect to product candidates and programs that involve technologies with which we have limited prior experience, such as those originally developed by Molecular Insight. Insufficient funds may require us to delay, scale back or eliminate some or all of our research and development programs, to lose rights under existing licenses or to relinquish greater or all rights to product candidates at an earlier stage of development or on less favorable terms than we would otherwise choose or may adversely affect our ability to operate as a going concern. We may not be able at the necessary time to obtain additional funding on acceptable terms, or at all. Our inability to raise additional capital on terms reasonably acceptable to us would seriously jeopardize our business.

If we are unable to negotiate collaboration agreements, our cash burn rate could increase and our rate of product development could decrease.

Our ability to generate revenue in the near term depends on the timing of achievement, if any, of certain payment triggering events under our existing collaboration agreements and our ability to enter into additional collaboration agreements with third parties. We may not be successful in negotiating additional collaboration arrangements with pharmaceutical and biotechnology companies to develop and commercialize product candidates and technologies. If we do not enter into new collaboration arrangements, we would have to devote more of our resources to clinical product development and product launch activities and to seeking additional sources of capital to fund those activities. If we were not successful in seeking such capital, our cash burn rate would increase or we would need to take steps to reduce our rate of product development. Our ability to enter into new collaborations may be dependent on many factors, such as the results of clinical trials, competitive factors and the fit of our programs with the risk tolerance of a potential collaborator, including in relation to regulatory issues, the patent portfolio, the clinical pipeline, the stage of the available data, overall corporate goals and financial position. If we are not able to generate revenue under our collaborations when and in accordance with our expectations or the expectations of industry analysts, this failure could harm our business and have an immediate adverse effect on the trading price of our common stock.

Drug development is a long and inherently uncertain process with a high risk of failure at every stage of development.

Drug development is a highly uncertain scientific and medical endeavor, and failure can unexpectedly occur at any stage of clinical development. Typically, there is a high rate of attrition for product candidates in preclinical and clinical trials due to scientific feasibility, safety, efficacy, changing standards of medical care and other variables. The risk of failure increases for our product candidates that are based on new technologies, as well as technologies with which we have limited prior experience, such as those originally developed by Molecular Insight. Pre-clinical studies and clinical trials are long, expensive and highly uncertain processes that can take many years. It will take us, or our collaborators, several years to complete clinical trials and the time required for completing testing and obtaining approvals is uncertain. The start or end of a clinical trial is often delayed or halted due to changing regulatory requirements, manufacturing challenges, required clinical trial administrative actions, slower than anticipated patient enrollment, changing standards of care, availability or prevalence of use of a comparator drug or required prior therapy, clinical outcomes, or our and our partners financial constraints. The FDA and other U.S. and foreign regulatory agencies have substantial discretion, at any phase of development, to terminate clinical trials, require additional clinical development or other testing, delay or withhold registration and marketing approval and mandate product withdrawals, including recalls. Results attained in early human clinical trials may not be indicative of results

in later clinical trials. In addition, many of our investigational or experimental drugs are at an early stage of development, and successful commercialization of early stage product candidates requires significant research, development, testing and approvals by regulators, and additional investment. Our products in the research or pre-clinical development stage may not yield results that would permit or justify clinical testing. Our failure to demonstrate adequately the safety and efficacy of a product under development would delay or prevent marketing approval, which could adversely affect our operating results and credibility. The failure of one or more of our product candidates could have a material adverse effect on our business, financial condition and results of operations.

Table of Contents

If we or our collaborators do not obtain regulatory approval for our product candidates on a timely basis, or at all, or if the terms of any approval impose significant restrictions or limitations on use, our business, results of operations and financial condition will be adversely affected. Setbacks in clinical development programs could have a material adverse effect on our business.

Regulatory approvals are necessary to market product candidates and require demonstration of a product s safety and efficacy through extensive pre-clinical and clinical trials. We or our collaborators may not obtain regulatory approval for product candidates on a timely basis, or at all, and the terms of any approval (which in some countries includes pricing approval) may impose significant restrictions, limitations on use or other commercially unattractive conditions. We, our collaborators or regulators may also amend, suspend or terminate clinical trials if we or they believe that the participating subjects are being exposed to unacceptable health risks, and after reviewing trial results, we or our collaborators may abandon projects which we previously believed to be promising for commercial or other reasons unrelated to patient risks. During this process, we may find, for example, that results of pre-clinical studies are inconclusive or not indicative of results in human clinical trials, clinical investigators or contract research organizations do not comply with protocols or applicable regulatory requirements, or that product candidates do not have the desired efficacy or have undesirable side effects or other characteristics that preclude marketing approval or limit their potential commercial use if approved. In such circumstances, the entire development program for that product candidate could be adversely affected, resulting in delays in trials or regulatory filings for further marketing approval and a possible need to reconfigure our clinical trial programs to conduct additional trials or abandon the program involved. Conducting additional clinical trials or making significant revisions to a clinical development plan would lead to delays in regulatory filings. If clinical trials indicate, or regulatory bodies are concerned about, actual or possible serious problems with the safety or efficacy of a product candidate, such as the concerns expressed in the FDA s July 2012 Complete Response Letter or during consideration of the oral Relistor development program, we or our collaborators may stop or significantly slow development or commercialization of affected products. As a result of such concerns, the development programs for subcutaneous and/or oral Relistor for chronic, non-cancer pain patients may be significantly delayed or terminated altogether.

Even if we agree to a path forward with Salix and the FDA, if the results of any future Relistor trials are not satisfactory or we or our collaborators encounter problems enrolling subjects, clinical trial supply issues, setbacks in developing drug formulations, including raw material-supply, manufacturing, stability or other difficulties, or issues complying with protocols or applicable regulatory requirements, the entire development program for Relistor could be adversely affected in a material manner. Such scenarios could also befall our other clinical-stage product candidates. If any of our collaborators breach or terminate its agreement with us or otherwise fail to conduct successfully and in a timely manner the collaborative activities for which they are responsible, the preclinical or clinical development or commercialization of the affected product candidate or research program could be delayed or terminated. We generally do not control the amount and timing of resources that our collaborators devote to our programs or product candidates. We also do not know whether current or future collaboration partners, if any, might pursue alternative technologies or develop alternative products either on their own or in collaboration with others, including our competitors, as a means for developing treatments for the diseases or conditions targeted by our collaborative arrangements. Setbacks of these types could have a material adverse effect on our business, results of operations and financial condition.

We or our collaborators must design and conduct successful clinical trials for our product candidates to obtain regulatory approval. We rely on third parties for conduct of clinical trials, which reduces our control over them and may expose us to conflicts of interest. Clinical trial results may be unfavorable or inconclusive, and often take longer than expected.

We have limited experience in conducting clinical trials, and we rely on or obtain the assistance of others to design, conduct, supervise or monitor some or all aspects of some of our clinical trials, including our ongoing phase 2 trials of PSMA ADC and MIP-1404. We have less control over the timing and other aspects of clinical trials for which we rely on third parties, such as contract research organizations, clinical data management organizations, medical institutions or clinical investigators, than if we conducted them entirely on our own. These third parties may also have relationships with other entities, some of which may be our competitors. In all events, we are responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. The FDA requires us to comply with good clinical practices for conducting and recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the

Table of Contents

rights, integrity and confidentiality of trial participants are protected. Our reliance on third parties that we do not control does not relieve us of these responsibilities and requirements.

To obtain regulatory approval of drug candidates, we must demonstrate through preclinical studies and clinical trials that they are safe and effective. Adverse or inconclusive clinical trial results concerning any of our drug candidates, or trials which regulators find deficient in scope, design or one or more other material respects, could require additional trials, resulting in increased costs, significant delays in submissions of approval applications, approvals in narrower indications than originally sought, or denials of approval, none of which we can predict. As a result, any projections that we publicly announce of commencement and duration of clinical trials are not certain. We have experienced clinical trial delays in the past as a result of slower than anticipated enrollment and such delays may recur. Delays can be caused by, among other things, deaths or other adverse medical events; regulatory or patent issues; interim or final results of ongoing clinical trials; failure to enroll clinical sites as expected; competition for enrollment from other clinical trials; scheduling conflicts with participating clinicians and institutions; disagreements, disputes or other matters arising from collaborations; our inability to obtain necessary funding; or manufacturing problems.

Under our license agreement, Salix generally has responsibility for conducting Relistor clinical trials, including all trials outside of the U.S. other than Japan, where Ono has the responsibility for clinical trials. In addition, certain clinical trials for our product candidates may be conducted by government-sponsored agencies, and consequently will be dependent on governmental participation and funding. These arrangements expose us to the same considerations we face when contracting with third parties for our own trials.

Our product candidates may not obtain regulatory approvals needed for marketing.

None of our product candidates, other than Relistor for the treatment of OIC in patients with advanced illnesses, has been approved by applicable regulatory authorities for marketing. The process of obtaining FDA and foreign regulatory approvals often takes many years and can vary substantially based upon the type, complexity and novelty of the products involved. We have had only limited experience in filing and pursuing applications and other submissions necessary to gain marketing approvals. Products under development may never obtain marketing approval from the FDA or other regulatory authorities necessary for commercialization.

Even if our product candidates obtain marketing approval, our ability to generate revenue will be diminished if our products are not accepted in the marketplace or our collaboration partners fail to obtain acceptable prices or an adequate level of reimbursement for products from third-party payors or government agencies.

The commercial success of our products will depend upon their acceptance by the medical community and third-party payors as clinically useful, cost effective and safe. Market acceptance of approved products, such as Relistor for patients with advanced illnesses, is affected by the timing of regulatory approvals, product launches and reimbursement programs for existing and expanded uses or generic, over-the-counter or other competitors; price increases for the product and relative prices of competing products; product development efforts for new indications; availability of sufficient commercial quantities of the product; success in arranging for necessary sublicense or distribution relationships; and general and industry-specific local and international economic pressures such as those experienced worldwide over the recent past. If health care providers believe that patients can be managed adequately with alternative, currently available therapies, they may not prescribe our products, especially if the alternative therapies are viewed as more effective, as having a better safety or tolerability profile, as being more convenient to the patient or health care providers or as being less expensive. Third-party insurance coverage may not be available to patients for any products we develop, alone or with collaborators. For pharmaceuticals administered in an institutional setting, the ability of the institution to be adequately reimbursed from government and health administration authorities, private health insurers and other third-party payors could also play a significant role in demand for our

products. Significant uncertainty exists as to the reimbursement status of newly-approved pharmaceuticals. Government and other third-party payors increasingly are attempting to contain healthcare costs by limiting both coverage and the level of reimbursement for new drugs and by refusing, in some cases, to provide coverage for uses of approved products for indications for which the FDA has not granted labeling approval. In some foreign markets, pricing and profitability of prescription pharmaceuticals are subject to government control. In the U.S., we expect that there will continue to be a number of federal and state proposals to implement similar government control and that the emphasis on managed care in the U.S. will continue to put pressure on the pricing of pharmaceutical products. Cost control initiatives could decrease the price that our collaborators receive for any

Table of Contents

products in the future and adversely affect the ability of our collaborators to commercialize our products and our realization of royalties from commercialization. If any of our products do not achieve market acceptance, we will likely lose our entire investment in that product.

Marketplace acceptance depends in part on competition in our industry, which is intense, and competing products in development may adversely affect acceptance of our products.

The extent to which any of our products achieves market acceptance will depend on competitive factors. Competition in the biopharmaceutical industry is intense and characterized by ongoing research and development and technological change. We face competition from many for-profit companies and major universities and research institutions in the U.S. and abroad. We face competition from companies marketing existing products or developing new products for diseases and conditions targeted by our technologies. We are aware of a number of products and product candidates, including ENTEREG® (alvimopan), AMITIZA® (lubiprostone), naloxegol, TD-1211 (in a phase 2 clinical testing by Theravance, Inc.), TARGIN® (oxycodone/naloxone), Zytiga® (abiraterone acetate), Xtandi® (enzalutamide), Alpharadin® (radium-223 chloride) and ProstaScint®, which compete or may potentially compete with Relistor, PSMA ADC or our other product candidates. For instance, there are product candidates in pre-clinical or clinical development that target the side effects of opioid pain therapy, and a marketed product for the treatment of post-operative ileus could compete with Relistor. We are aware of several competitors, including Janssen Biotech, Inc., Medivation, Inc., Algeta ASA and Jazz Pharmaceuticals Public Limited Company, which have received approval for or are developing alternative treatments or diagnostics for castration-resistant prostate cancer, some of which are directed against PSMA, and others, including MedImmune/Auven Therapeutics Spirogen, which are developing ADCs as oncology therapeutics. Any of these competing approved products or product candidates, or others which may be developed in the future, may achieve a significant competitive advantage relative to Relistor, PSMA ADC, MIP-1404 or any of our other product candidates.

Competition with respect to our technologies and products is based on, among other things, product efficacy, safety, reliability, method of administration, availability, price and clinical benefit relative to cost; timing and scope of regulatory approval; sales, marketing and manufacturing capabilities; collaborator capabilities; insurance and other reimbursement coverage; and patent protection. Competitive disadvantages in any of these factors could materially harm our business and financial condition. Many of our competitors have substantially greater research and development capabilities and experience and greater manufacturing, marketing, financial and managerial resources than we do. These competitors may develop products that are superior to those we are developing and render our products or technologies non-competitive or obsolete. Our products and product candidates under development may not compete successfully with existing products or product candidates under development by other companies, universities and other institutions. Drug manufacturers that are first in the market with a therapeutic for a specific indication generally obtain and maintain a significant competitive advantage over later entrants and therefore, the speed with which industry participants move to develop products, complete clinical trials and approval processes and commercialize products is an important competitive factor. If our product candidates receive marketing approval but cannot compete effectively in the marketplace, our operating results and financial position would suffer.

If we or our collaborators are unable to obtain sufficient quantities of the raw and bulk materials needed to make our product candidates or Relistor, development of our product candidates or commercialization of our approved product could be slowed or stopped.

Salix or Ono may not be able to fulfill manufacturing obligations for Relistor, either on their own or through third-party suppliers. A delay or disruption of supplies of Relistor would have a material adverse effect on the Relistor franchise, and therefore on our business as a whole. Our existing arrangements with suppliers for our other product candidates may not result in the supply of sufficient quantities of our product candidates needed to accomplish our

clinical development programs, and we may not have the right and in any event do not currently have the capability to manufacture these products if our suppliers are unable or unwilling to do so. We currently arrange for supplies of critical raw materials used in production of our product candidates from single sources. We do not have long-term contracts with any of these suppliers. Any delay or disruption in the availability of raw materials would slow or stop product development and commercialization of the relevant product.

Table of Contents

Manufacturing resources could limit or adversely affect our ability to commercialize products.

We or our collaborators engage third parties to manufacture our approved product and product candidates. We or our collaborators may not be able to obtain adequate supplies from third-party manufacturers in a timely fashion for development or commercialization purposes, and commercial quantities of products may not be available from contract manufacturers at acceptable costs. Under our license agreement with Salix, Salix is responsible for obtaining supplies of Relistor, including contracting with contract manufacturing organizations for supply of Relistor active pharmaceutical ingredient and subcutaneous and oral finished drug product. These arrangements may not be on terms that are advantageous and, as a result of our royalty and other interests in Relistor s commercial success, will subject us to risks that the counterparties may not perform optimally in terms of quality or reliability. In engaging third parties for these activities, we do not control many aspects of the manufacturing process, including compliance with current Good Manufacturing Practices (cGMP) and other regulatory requirements. In order to commercialize our product candidates successfully, we or our collaborators need to be able to manufacture or arrange for the manufacture of products in commercial quantities, in compliance with regulatory requirements, at acceptable costs and in a timely manner. Manufacture of our product candidates can be complex, difficult to accomplish even in small quantities, difficult to scale-up for large-scale production and subject to delays, inefficiencies and low yields of quality products. The cost of manufacturing some of our product candidates may make them prohibitively expensive. If adequate supplies of any of our product candidates or related materials are not available on a timely basis or at all, our clinical trials could be seriously delayed, since these materials are time consuming to manufacture and cannot be readily obtained from third-party sources. If we were to decide to establish a commercial-scale manufacturing facility in the future, we would require substantial additional funds and be required to hire and train significant numbers of employees and comply with applicable regulations.

Failure of any manufacturer of Relistor or our product candidates to comply with applicable regulatory requirements could subject us to penalties and have a material adverse effect on supplies of our product or product candidates.

Third-party manufacturers are required to comply with cGMP or similar regulatory requirements outside of the U.S. If manufacturers of our product or product candidates cannot successfully manufacture material that conforms to the strict regulatory requirements of the FDA and any applicable foreign regulatory authority, they may not be able to obtain any required approval for their manufacturing facilities. If these facilities are not approved for commercial manufacture, we may need to find alternative manufacturing facilities, which could result in delays of several years in obtaining approval for a product candidate. We do not control the manufacturing process and are completely dependent on our third-party manufacturing partners or contractors for compliance with the applicable regulatory requirements for the manufacture of Relistor and our product candidates. Manufacturers are subject to ongoing periodic unannounced inspections by the FDA and corresponding state and foreign agencies for compliance with cGMP and similar regulatory requirements. Failure of any manufacturer of Relistor or any of our product candidates to comply with applicable cGMP or other regulatory requirements could result in sanctions being imposed on our collaborators or us, including fines, injunctions, civil penalties, delays, suspensions or withdrawals of approvals, operating restrictions, interruptions in supply and criminal prosecutions, any of which could significantly and adversely affect supplies of Relistor or such product candidate and have a material adverse impact on our business, financial condition and results of operations.

We are dependent on patents and other intellectual property rights. The validity, enforceability and commercial value of our patents and other intellectual property rights are highly uncertain.

We own or have direct or sub-licenses to a number of issued patents. We must obtain, maintain and enforce patent and other rights to protect our intellectual property. The patent position of biotechnology and pharmaceutical firms is

highly uncertain and involves many complex legal and technical issues. There are many laws, regulations and judicial decisions that dictate and otherwise influence the manner in which patent applications are filed and prosecuted and in which patents are granted and enforced, all of which are subject to change from time to time. There is no clear policy involving the breadth of claims allowed, or the degree of protection afforded, under patents in this area. In addition, we are aware of others who have patent applications or patents containing claims similar to or overlapping those in our patents and patent applications. Accordingly, patent applications owned by or licensed to us may not result in patents being issued. Even if we own or license a relevant issued patent, we may not be able to preclude competitors from commercializing drugs that may compete directly with one or more of our products or product candidates, in which event such rights may not provide us with any meaningful competitive advantage.

Table of Contents

In the absence or upon successful challenge of patent protection, drugs may be subject to generic competition, which could adversely affect pricing and sales volumes of the affected products.

It is generally difficult to determine the relative strength or scope of a biotechnology or pharmaceutical patent position in absolute terms at any given time. The issuance of a patent is not conclusive as to its validity or enforceability, which can be challenged in litigation or via administrative proceedings. The license agreements from which we derive or out-license intellectual property provide for various royalty, milestone and other payment, commercialization, sublicensing, patent prosecution and enforcement, insurance, indemnification and other obligations and rights, and are subject to certain reservations of rights. While we generally have the right to defend and enforce patents licensed to or by us, either in the first instance or if the licensor or licensee chooses not to do so, we must usually bear the cost of doing so. Under our license agreement with Salix, Salix generally has the first right to control the defense and enforcement of our Relistor patents. With respect to Japan, Ono has certain limited rights to prosecute, maintain and enforce relevant intellectual property. We may incur substantial costs in seeking to uphold the validity of patents or to prevent infringement. If the outcome of a dispute or contest is adverse to us, third parties may be able to use our patented invention without payment to us. Third parties may also avoid our patents through design innovation.

Patents have a limited life and expire by law.

In addition to uncertainties as to scope, validity, enforceability and changes in law, patents by law have limited lives. Upon expiration of patent protection, our drug candidates and/or products may be subject to generic competition, which could adversely affect pricing and sales volumes of the affected products.

With respect to PSMA ADC, currently issued composition-of-matter patents comprising co-owned and in-licensed properties have expiration ranges of 2022 to 2023 in the U.S. and 2022 to 2026 ex-U.S. Corresponding patent applications as well as patent applications directed to methods of use (except for the U.S. patent expiring in 2023) are pending worldwide, which if issued would have expiration ranges from 2022 to 2029. We view all of these patents as significant.

Owned and in-licensed properties relating to the MIP-1404 product candidate have expiration ranges of 2020 to 2029; we view as most significant the composition-of-matter patent on the compound, as well as technetium-99 labeled forms, which expires in 2029. Additional U.S. patents are directed to various inventions relating to the product candidate, and corresponding patent applications are pending worldwide.

With regard to our Relistor-related intellectual property, the composition-of-matter patent for the active ingredient of Relistor, methylnaltrexone, was invented in the 1970 s and has expired. The University of Chicago, as well as Progenics and its collaborators, have extended the methylnaltrexone patent estate with additional patents and pending patent applications covering various inventions relating to the product. Salix has listed in the FDA Orange Book four U.S. patents relating to subcutaneous Relistor, which have expiration dates ranging from 2017 to 2030, and one patent (expiring in 2024) with Health Canada. A patent issued in September 2013 provides protection for the oral methylnaltrexone product until 2031.

We depend on intellectual property licensed from third parties and unpatented technology, trade secrets and confidential information. If we lose any of these rights, including by failing to achieve milestone requirements or to satisfy other conditions, or if they or data embodying or relevant to them are compromised by disruptions or breaches of information or data security, our business, results of operations and financial condition could be harmed.

Most of our product candidates, including Relistor, incorporate intellectual property licensed from third parties. For example, PSMA ADC utilizes technology licensed to us from Sloan-Kettering Institute for Cancer Research, through Cytogen Corporation, and Seattle Genetics, Inc. We can lose the right to patents and other intellectual property licensed to us if the related license agreement is terminated due to a breach by us or otherwise. Our ability, and that of our collaboration partners, to commercialize products incorporating licensed intellectual property would be impaired if the related license agreements were terminated. In addition, we are required to make substantial cash payments, achieve milestones and satisfy other conditions, including filing for and obtaining marketing approvals and introducing products, to maintain rights under our intellectual property licenses. Due to the nature of these agreements and the uncertainties of research and development, we may not be able to achieve milestones or satisfy conditions to which we have contractually committed, and as a result may be unable to maintain our rights under

these licenses. If we do not comply with our license agreements, the licensors may terminate them, which could result in our losing our rights to, and therefore being unable to commercialize, related products.

We also rely on unpatented technology, trade secrets and confidential information. Third parties may independently develop substantially equivalent information and techniques or otherwise gain access to our technology or disclose our technology, and we may be unable to effectively protect our rights in unpatented technology, trade secrets and confidential information. We require each of our employees, consultants and advisors to execute a confidentiality agreement at the commencement of an employment or consulting relationship with us. These agreements may, however, not provide effective protection in the event of unauthorized use or disclosure of confidential information. Any loss of trade secret protection or other unpatented technology rights could harm our business, results of operations and financial condition.

Progenics and other businesses and organizations worldwide, and in particular technology-intensive activities such as biotechnology research and development, are increasingly dependent on critical, complex and interdependent information technology systems, including Internet-based systems, to facilitate or perform basic research and development functions, business processes, internal and external communications, and other critical functions. Progenics relies on such systems for most aspects of its business. The size and complexity of computer, communications and other electronic networked data generation, storage and transfer systems make them potentially vulnerable to breakdown, malicious intrusion, computer viruses and data security breaches by unauthorized third parties, employees or others. Such events may permit unauthorized persons to access, misappropriate and/or destroy sensitive data and result in the impairment or disruption of important business processes, loss of trade secrets or other proprietary intellectual property or public exposure of personal information (including sensitive personal information) of employees, business partners, clinical trial patients, customers and others. Any of the foregoing could have a material adverse effect on our business, prospects, operating results, and financial condition.

If we do not achieve milestones or satisfy conditions regarding some of our product candidates, we may not maintain our rights under related licenses.

We are required to make substantial cash payments, achieve milestones and satisfy other conditions, including filing for and obtaining marketing approvals and introducing products, to maintain rights under our intellectual property licenses. Due to the nature of these agreements and the uncertainties of research and development, we may not be able to achieve milestones or satisfy conditions to which we have contractually committed, and as a result may be unable to maintain our rights under these licenses. If we do not comply with our license agreements, the licensors may terminate them, which could result in our losing our rights to, and therefore being unable to commercialize, related products.

If we infringe third-party patent or other intellectual property rights, we may need to alter or terminate a product development program.

There may be patent or other intellectual property rights belonging to others that require us to alter our products, pay licensing fees or cease certain activities. If our products infringe patent or other intellectual property rights of others, the owners of those rights could bring legal actions against us claiming damages and seeking to enjoin manufacturing and marketing of the affected products. If these legal actions are successful, in addition to any potential liability for damages, we could be required to obtain a license in order to continue to manufacture or market the affected products. We may not prevail in any action brought against us, and any license required under any rights that we infringe may not be available on acceptable terms or at all. We are aware of intellectual property rights held by third parties that relate to products or technologies we are developing. For example, we are aware of other groups investigating PSMA or related compounds, monoclonal antibodies directed at PSMA and targets relevant to PSMA ADC, and

methylnaltrexone and other peripheral opioid antagonists, and of patents held, and patent applications filed, by these groups in those areas. While the validity of these issued patents, patentability of these pending patent applications and applicability of any of them to our programs are uncertain, if asserted against us, any related patent or other intellectual property rights could adversely affect our ability to commercialize our products.

Research, development and commercialization of a biopharmaceutical often requires choosing between alternative development and optimization routes at various stages in the development process. Preferred routes depend on subsequent discoveries and test results and cannot be predicted with certainty at the outset. There are numerous

Table of Contents

third-party patents in our field, and we may need to obtain a license under a patent in order to pursue the preferred development route of one or more of our products or product candidates. The need to obtain a license would decrease the ultimate profitability of the applicable product. If we cannot negotiate a license, we might have to pursue a less desirable development route or terminate the program altogether.

We are dependent upon third parties for a variety of functions. These arrangements may not provide us with the benefits we expect.

We rely on third parties to perform a variety of functions. We are party to numerous agreements which place substantial responsibility on clinical research organizations, consultants and other service providers for the development of our approved product and our product candidates. We also rely on medical and academic institutions to perform aspects of our clinical trials of product candidates. In addition, an element of our research and development strategy has been to in-license technology and product candidates from academic and government institutions in order to minimize investments in early research. We have entered into agreements under which we are now dependent on Ono and Salix for the commercialization and development of Relistor. We may not be able to maintain our relationships with them or establish new ones for Relistor or other product candidates on beneficial terms. We may not be able to enter new arrangements without undue delays or expenditures, and these arrangements may not allow us to compete successfully. Moreover, if third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct clinical trials in accordance with regulatory requirements or applicable protocols, our product candidates may not be approved for marketing and commercialization or such approval may be delayed. If that occurs, we or our collaborators will not be able, or may be delayed in our efforts, to commercialize our product candidates.

We lack sales and marketing infrastructure and related staff, which will require significant investment to establish and in the meantime may make us dependent on third parties for their expertise in this area.

We have no established sales, marketing or distribution infrastructure. If we receive marketing approval for a pharmaceutical product, significant investment, time and managerial resources will be required to build the commercial infrastructure required to market, sell and support it. Should we choose to commercialize a product directly, we may not be successful in developing an effective commercial infrastructure or in achieving sufficient market acceptance. Alternatively, we may choose to market and sell products through distribution, co-marketing, co-promotion or licensing arrangements with third parties. We may also consider contracting with a third party professional pharmaceutical detailing and sales organization to perform the marketing function for one or more products. To the extent that we enter into distribution, co-marketing, co-promotion, detailing or licensing arrangements for the marketing and sale of product candidates, any revenue we receive will depend primarily on the efforts of third parties. We will not control the amount and timing of marketing resources these third parties devote to our products.

We are exposed to product liability claims, and in the future may not be able to obtain insurance against claims at a reasonable cost or at all.

Our business exposes us to product liability risks, which are inherent in the testing, manufacturing, marketing and sale of pharmaceutical products. We may not be able to avoid product liability exposure. If a product liability claim is successfully brought against us, our financial position may be adversely affected. Under our license agreement with Salix, we are responsible for product liability claims arising out of clinical trials that were conducted under our supervision. We are indemnified by Salix under our license agreement with Salix for product liability exposure arising from its marketing and sales of Relistor, and maintain our own product liability insurance coverage in the amount of $10.0 million per occurrence, subject to a deductible and a $10.0 million annual aggregate limitation and other clinical trial or other insurance as required by contract and local laws. Pursuant to our transition agreement with Wyeth

Pharmaceuticals, we released Wyeth from its indemnification responsibility for product liability exposure arising from its marketing and sales of Relistor. Product liability insurance for the biopharmaceutical industry is generally expensive, when available at all, and may not be available to us at a reasonable cost in the future. Our current insurance coverage and indemnification arrangements may not be adequate to cover claims brought against us, and are in any event subject to the insuring or indemnifying entity discharging its obligations to us.

Table of Contents

We handle hazardous materials and must comply with environmental laws and regulations, which can be expensive and restrict how we do business. If we are involved in a hazardous waste spill or other accident, we could be liable for damages, penalties or other forms of censure.

Our research and development work and manufacturing processes involve the use of hazardous, controlled and radioactive materials. We are subject to federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of these materials. Despite procedures that we implement for handling and disposing of these materials, we cannot eliminate the risk of accidental contamination or injury. In the event of a hazardous waste spill or other accident, we could be liable for damages, penalties or other forms of censure. We may be required to incur significant costs to comply with environmental laws and regulations in the future.

If we lose key management and scientific personnel on whom we depend, our business could suffer.

We are dependent upon our key management and scientific personnel, the loss of whom could require us to identify and engage qualified replacements, and could cause our management and operations to suffer in the interim. Competition for qualified employees among companies in the biopharmaceutical industry is intense. Future success in our industry depends in significant part on the ability to attract, retain and motivate highly skilled employees, which we may not be successful in doing.

Heath care reform measures could adversely affect our operating results and our ability to obtain marketing approval of and to commercialize our product candidates.

In the U.S. and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the health care system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval. Legislative and regulatory proposals 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 significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements. In the U.S., federal legislation has changed the way Medicare covers and pays for pharmaceutical products. Cost reduction initiatives and other provisions of legislation have decreased coverage and reimbursement. Though such legislation applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. More recent legislation is intended to broaden access to health insurance, further reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for health care and health insurance industries, and impose new taxes and fees on the health industry and additional health policy reforms. New laws impose significant annual fees on companies that manufacture or import branded prescription drug products, and contain substantial new compliance provisions, which in each case may affect our business practices with health care practitioners. Subject to federal and state agencies issuing regulations or guidance, it appears likely that new laws will continue to pressure pharmaceutical pricing, especially under the Medicare program, and may also increase regulatory burdens and operating costs. We cannot be sure whether additional legislative changes will be enacted, whether the FDA regulations, guidance or interpretations will be changed or what the impact of such changes on the marketing approvals of our product candidates, if any, may be.

Our and/or our collaborators relationships with customers and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us or them to criminal sanctions, civil penalties, program exclusion, contractual damages, reputational harm and diminished profits and future earnings.

Health care providers, physicians and third-party payors play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our or our collaborators future arrangements with third-party payors and customers may expose us or them to broadly applicable fraud and abuse and other health care laws and regulations that may constrain the business or financial arrangements and relationships through which we or our collaborators market, sell and distribute our products that obtain marketing approval. Efforts to ensure that business arrangements comply with applicable health care laws and regulations involve substantial costs. It is possible that governmental authorities will conclude that our or our collaborators business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If such operations are found to be in violation of any of these laws or other applicable governmental regulations, we or the collaborator may be subject to significant civil, criminal and administrative penalties,

Table of Contents

damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of related operations. If physicians or other providers or entities involved with our products are found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs, which may adversely affect us.

We cannot rely on federal government grants and research contracts as a continuing source of funds.

Federal government grants and research contracts, in particular from the National Institutes of Health, have in the past generally been available for biotechnology research and development in various areas. Funds available under such grants or contracts, however, must be applied for, if awarded must be used to fund qualifying research and development programs specified in the application, and are subject to adjustment based on the results of periodic audits. The government s obligation to make payments under these grants and/or contracts is subject to appropriation by the U.S. Congress for funding in each year, which is subject to changes due to budgetary constraints, policy changes and other factors. While we have been awarded such grants and contracts in the past, we do not currently have significant funding from such sources, and in any event cannot rely on them as a continuing source of funds.

Our future depends on the proper management of our current and future business operations, including those of Molecular Insight, and their associated expenses.

Our business strategy requires us to manage our business to provide for the continued development and potential commercialization of our proprietary and partnered product candidates. Our strategy also calls for us to undertake increased research and development activities and to manage an increasing number of relationships with partners and other third parties, while simultaneously managing the capital necessary to support this strategy. These tasks are significantly increased as a result of our acquisition of Molecular Insight. If we are unable to manage effectively our current operations and any growth we may experience, our business, financial condition and results of operations may be adversely affected. If we are unable to effectively manage our expenses, we may find it necessary to reduce our personnel-related costs through reductions in our workforce, which could harm our operations, employee morale and impair our ability to retain and recruit talent. Furthermore, if adequate funds are not available, we may be required to obtain funds through arrangements with partners or other sources that may require us to relinquish rights to certain of our technologies, products or future economic rights that we would not otherwise relinquish or require us to enter into other financing arrangements on unfavorable terms.

Progenics has a history of operating losses, as does Molecular Insight, which has also been reorganized under the U.S. Bankruptcy Code.

Progenics has incurred substantial losses throughout its history. A large portion of our revenue has historically consisted of upfront and milestone from licensing transactions. We have reported operating losses for the nine months ended September 30, 2013 and for the twelve months ended December 31, 2012 and, while we reported operating income for 2011 as a result of a one-time upfront payment from Salix, the timing and amount of any similar transactions in the future is highly unpredictable and uncertain. Without upfront or other such payments, we operate at a loss, due in large part to the significant research and development expenditures required to identify and validate new product candidates and pursue our development efforts. Moreover, we have derived no significant revenue from product sales and have only in the last several years derived revenue from royalties. We may not achieve significant product sales or royalty revenue for a number of years, if ever. We expect to incur net operating losses and negative cash flow from operations in the future, which could increase significantly if we expand our clinical trial programs and other product development efforts, including those attendant to the product candidates and programs originally developed by Molecular Insight. Our ability to achieve and sustain profitability is dependent in part on obtaining

regulatory approval for and then commercializing our product candidates, either alone or with others. We may not be able to develop and commercialize products beyond subcutaneous Relistor for OIC in patients with advanced illness. Our operations may not be profitable even if any of our other product candidates under development are commercialized.

Molecular Insight incurred net losses every year from its inception in 1997 and generated no significant revenue from product sales and only limited revenue from licenses. In December 2010, Molecular Insight filed a voluntary petition in the United States Bankruptcy Court for the District of Massachusetts seeking relief under the provisions of Chapter 11 of the U.S. Bankruptcy Code (Case No. 10-23355). It operated its business and managed its properties as a debtor in possession under bankruptcy protection until emerging from bankruptcy in May 2011.

Table of Contents

Our ability to use net operating losses to offset future taxable income is subject to certain limitations.

We currently have significant net operating losses (NOLs) that may be used to offset future taxable income. The U.S. Internal Revenue Code limits the amount of taxable income that may be offset annually by NOL carryforwards after a change in control (generally greater than 50% change in ownership) of a loss corporation, and our use of NOL carryforwards may be further limited as a result of any future equity transactions that result in an additional change of control.

Risks Related to this Offering and our Common Stock

Management will have broad discretion as to the use of the proceeds from this offering, and we may not use the proceeds effectively.

Our management will have broad discretion in the application of the net proceeds from this offering and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. Our failure to apply these funds effectively could significantly harm our business or the development of our product candidates and decrease the price of your common stock.

Progenics stock price has a history of volatility and may be affected by selling pressure, including in the event of substantial sales of Progenics stock by former Molecular Insight stockholders. You should consider an investment in Progenics stock as risky and invest only if you can withstand a significant loss.

Our stock price has a history of significant volatility. The sales price of our common stock varied between a high price of $6.47 and a low of $2.53 in 2013 and between a high price of $7.45 and a low price of $4.26 from January 2, 2014 through February 20, 2014. Factors that may have a significant impact on the market price of our common stock include the results of clinical trials and pre-clinical studies undertaken by us or others; delays, terminations or other changes in development programs; developments in marketing approval efforts, such as the FDA s July 2012 Complete Response Letter with respect to the sNDA for Relistor subcutaneous injection for the treatment of OIC in adult patients with chronic, non-cancer pain; developments in collaborator or other business relationships, particularly regarding Relistor, PSMA ADC or other significant products or programs; technological innovation or product announcements by us, our collaborators or our competitors; patent or other proprietary rights developments; governmental regulation; changes in reimbursement policies or health care legislation; safety and efficacy concerns about products developed by us, our collaborators or our competitors; our ability to fund ongoing operations; fluctuations in our operating results; and general market conditions. At times, our stock price has been volatile even in the absence of significant news or developments. The stock prices of biotechnology companies and securities markets generally have been subject to dramatic price swings in recent years, and financial and market conditions during that period have resulted in widespread pressures on securities of issuers throughout the world economy.

Investors in this offering will experience immediate and substantial dilution in the net tangible book value per share of the common stock they purchase.

Since the price per share of our common stock being offered is higher than the net tangible book value per share of our common stock, you will suffer substantial dilution in the net tangible book value of the common stock you purchase in this offering. See Dilution for a more detailed discussion of the dilution you will incur if you purchase common stock in this offering.

Our stockholders may be diluted, and the price of our common stock may decrease, as a result of future issuances of securities or the exercise of outstanding stock options or other convertible or exercisable securities.

We expect to issue additional common stock and options to purchase common stock, and may issue preferred stock, restricted stock units or securities convertible into or exercisable or exchangeable for our common stock. Sales of substantial numbers of outstanding shares of common stock, including sales by former Molecular Insight stockholders of unregistered shares that have been issued in the acquisition and may be released from the share escrow which expires in April 2014, could also cause a decline in the market price of our stock. We require substantial external funding to finance our research and development programs and may seek such funding through the issuance and sale of our common stock. We filed a shelf registration statement with the SEC on January 23, 2014, which was declared effective by the SEC on February 5, 2014. The shelf registration statement may be used to sell an aggregate of up to $150 million of shares of our common stock and other securities, including the amount to be sold in this offering and up to $50 million of shares of common stock that may be sold and issued by us, from

Table of Contents

time to time, through at-the-market offerings pursuant to the Controlled Equity Offering℠ Sales Agreement we entered with Cantor Fitzgerald & Co. on January 23, 2014. As of the date of this prospectus supplement, we have not sold any shares of common stock under such sales agreement with Cantor Fitzgerald & Co.

We also have registration statements on file with the SEC registering shares issuable pursuant to our equity compensation plans. Sales of our securities pursuant to these registration statements could cause the market price or our stock to decline. Furthermore, any sales by existing stockholders or holders of options, or other rights, may have an adverse effect on our ability to raise capital and may adversely affect the market price of our common stock. Shares of common stock for which our outstanding stock options are exercisable are eligible for immediate sale in the public market after purchase. The issuance of additional common stock, preferred stock, restricted stock units or other securities convertible into or exchangeable or exercisable for our common stock or the exercise of stock options would dilute existing investors and could lower the price of our common stock.

Our principal stockholders are able to exert significant influence over matters submitted to stockholders for approval.

As of December 31, 2013, our directors and executive officers together beneficially owned or controlled approximately six percent of our outstanding shares of common stock, including shares that may be purchased upon exercise of outstanding stock options held by them within 60 days after December 31, 2013, and our five largest other stockholders beneficially owned or controlled approximately 52 percent of our outstanding shares of common stock based on their Schedules 13G filed with the SEC. Should these parties choose to act alone or together, they could exert significant influence in determining the outcome of corporate actions requiring stockholder approval and otherwise control our business. This control could, among other things, have the effect of delaying or preventing a change in control of the Company, adversely affecting our stock price.

We have never paid dividends on our common stock and we do not anticipate paying cash dividends on our common stock in the foreseeable future.

We have never declared or paid cash dividends on our common stock. We do not anticipate paying any cash dividends on our common stock in the foreseeable future. We currently intend to retain all available funds and any future earnings to fund the development and growth of our business. As a result, capital appreciation, if any, of our common stock will be the sole source of gain for the foreseeable future for holders of our common stock.

Anti-takeover provisions may make removal of our Board and/or management more difficult, discouraging hostile bids for control that may be beneficial to our stockholders.

Our Board is authorized, without further stockholder action, to issue from time to time shares of preferred stock in one or more designated series or classes. The issuance of preferred stock, as well as provisions in some outstanding stock options that provide for acceleration of exercisability upon a change of control, and Section 203 and other provisions of the Delaware General Corporation Law could make a takeover or the removal of our Board or management more difficult; discourage hostile bids for control in which stockholders may receive a premium for their shares; and otherwise dilute the rights of common stockholders and depress the market price of our stock.

Table of Contents

SPECIAL NOTE REGARDING FORWARD LOOKING STATEMENTS

Certain statements contained or incorporated by reference in this prospectus supplement and the accompanying prospectus constitute forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act of 1995 and releases issued by the SEC and within the meaning of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act of 1934, as amended (Exchange Act). From time to time, we publish forward-looking statements relating to matters such as anticipated financial performance, business prospects, technological developments, new products, research and development activities and other aspects of our present and future business operations as well as similar matters.

Forward-looking statements involve known and unknown risks and uncertainties which may cause our actual results, performance or achievements to be materially different from those expressed or implied by forward-looking statements. While it is impossible to identify or predict all such matters, these differences may result from, among other things, the inherent uncertainty of the timing and success of, and expense associated with, research, development, regulatory approval and commercialization of our products and product candidates, including the risks that clinical trials will not commence or proceed as planned; products appearing promising in early trials will not demonstrate efficacy or safety in larger-scale trials; clinical trial data on our products and product candidates will be unfavorable; our products will not receive marketing approval from regulators or, if approved, do not gain sufficient market acceptance to justify development and commercialization costs; competing products currently on the market or in development might reduce the commercial potential of our products; we, our collaborators or others might identify side effects after the product is on the market; or efficacy or safety concerns regarding marketed products, whether or not originating from subsequent testing or other activities by us, governmental regulators, other entities or organizations or otherwise, and whether or not scientifically justified, may lead to product recalls, withdrawals of marketing approval, reformulation of the product, additional pre-clinical testing or clinical trials, changes in labeling of the product, the need for additional marketing applications, declining sales or other adverse events.

We are also subject to risks and uncertainties associated with our integration of the product candidates, research and development and operations of Molecular Insight; the actions of our corporate, academic and other collaborators and government regulatory agencies, including risks from market forces and trends; potential product liability; intellectual property, litigation and other dispute resolution, environmental and other risks; the risk that we may not be able to enter into favorable collaboration or other relationships or that existing or future relationships may not proceed as planned; the risk that current and pending patent protection for our products may be invalid, unenforceable or challenged, or fail to provide adequate market exclusivity, or that our rights to in-licensed intellectual property may be terminated for our failure to satisfy performance milestones; the risk of difficulties in, and regulatory compliance relating to, manufacturing products; and the uncertainty of our future profitability.

Risks and uncertainties also include general economic conditions, including interest and currency exchange-rate fluctuations and the availability of capital; changes in generally accepted accounting principles; the impact of legislation and regulatory compliance; the highly regulated nature of our business, including government cost-containment initiatives and restrictions on third-party payments for our products; trade buying patterns; the competitive climate of our industry; and other factors set forth in this document and other reports filed with the SEC. In particular, we cannot assure you that Relistor® will be commercially successful or be approved in the future in other formulations, indications or jurisdictions, or that any of our other programs will result in a commercial product.

Please see Risk Factors in this prospectus supplement for additional information concerning these and other risks and uncertainties.

In some cases, you can identify forward-looking statements by terminology such as expect, anticipate, estimate, plan believe, could, intend, predict, may, should, will and words of similar import regarding our expectations. Forward-looking statements are only predictions and actual events or results may differ materially. Although we believe that our expectations are based on reasonable assumptions within the bounds of our current knowledge of our industry, business and operations, we cannot guarantee that actual results will not differ materially from our expectations. In evaluating such forward-looking statements, you should specifically consider various factors, including the risks outlined under the heading Risk Factors contained in this prospectus

Table of Contents

supplement and the accompanying prospectus, and in our 2012 Annual Report on Form 10-K, particularly in Amendment No. 2 thereto filed on January 17, 2014, and in our most recent Quarterly Reports on Form 10-Q and Current Reports on Form 8-K filed with the SEC. The discussion of risks and uncertainties set forth in those filings is not necessarily a complete or exhaustive list of all risks facing us at any particular point in time. We operate in a highly competitive, highly regulated and rapidly changing environment, and our business is in a state of evolution. Therefore, it is likely that over time new risks will emerge and the nature and elements of existing risks will change. It is not possible for management to predict all such risk factors or changes therein or to assess either the impact of all such risk factors on our business or the extent to which any individual risk factor, combination of factors or new or altered factors may cause results to differ materially from those contained in any forward-looking statement. Forward-looking statements represent our estimates and assumptions only as of the date such forward-looking statements are made. You should carefully read this prospectus supplement and the accompanying prospectus, together with the information incorporated herein or therein by reference, and with the understanding that our actual future results may materially differ from what we expect.

Except as required by law, forward-looking statements speak only as of the date they are made. We do not have a policy of updating or revising forward-looking statements and we assume no obligation to update any statements as a result of new information or future events or developments. It should not be assumed that our silence over time means that actual events are bearing out as expressed or implied in forward-looking statements.

Table of Contents

USE OF PROCEEDS

We estimate that the net proceeds from the sale of the 7,608,696 shares of common stock that we are offering will be approximately $32.6 million, or approximately $37.5 million if the underwriters exercise in full their option to purchase 1,141,304 additional shares of common stock, based on the public offering price of $4.60 per share and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

We intend to use the net proceeds from this offering for research and development and general corporate purposes. We may also use a portion of the net proceeds to acquire, license or invest in businesses, products, product candidates, technologies, intellectual property or other assets that are complementary to our own. We regularly consider such opportunities, but have no current understandings, agreements or commitments to effect any such transaction.

The amounts and timing of our actual expenditures depend on a number of factors, including the timing, scope, progress and results of our research and development efforts, the results of clinical trials and other studies, the timing and progress of any partnering efforts, the competitive environment for our products and product candidates and any unforeseen cash needs. Successful development of product candidates is highly uncertain and may not result in approved products. Completion dates and completion costs can vary significantly for each product candidate and are difficult to predict. As of the date of this prospectus supplement, we cannot specify with certainty all of the particular uses of the proceeds from this offering. Accordingly, we will have broad discretion in the use of the net proceeds from this offering and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our stock.

Pending the application of the net proceeds as described above, we may invest the net proceeds in short-term, interest-bearing instruments or other investment-grade securities, certificates of deposit or short-term U.S. government securities.

Table of Contents

DILUTION

Our net tangible book value as of September 30, 2013 was approximately $46.9 million, or $0.77 per share of our common stock. Net tangible book value per share is determined by dividing our total tangible assets, less total liabilities, by the number of shares of our common stock outstanding as of September 30, 2013. Dilution in net tangible book value per share represents the difference between the amount per share paid by purchasers of shares of common stock in this offering and the as adjusted net tangible book value per share of our common stock immediately after this offering.

After giving effect to the sale of 7,608,696 shares of our common stock in this offering at the public offering price of $4.60 per share and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of September 30, 2013 would have been approximately $79.5 million, or $1.16 per share. This represents an immediate increase in net tangible book value of $0.39 per share to existing stockholders and immediate dilution in net tangible book value of $3.44 per share to new investors purchasing our common stock in this offering. The following table illustrates this dilution on a per share basis:

Public offering price per share		$ 4.60
Net tangible book value per share as of September 30, 2013	$ 0.77	
Increase per share attributable to new investors	0.39	
As adjusted net tangible book value per share as of September 30, 2013 after this offering		1.16
Dilution in net tangible book value per share to new investors		$ 3.44

If the underwriters exercise in full their option to purchase 1,141,304 additional shares of common stock at the public offering price of $4.60 per share, the as adjusted net tangible book value after this offering would be $1.21 per share of common stock, representing an increase in net tangible book value of $0.44 per share to existing stockholders and immediate dilution in net tangible book value of $3.39 per share to new investors purchasing our common stock in this offering.

The number of shares of our common stock to be outstanding immediately after this offering is based on 60,825,404 shares outstanding as of September 30, 2013, and excludes as of such date:

- 5,458,254 shares of our common stock issuable upon the exercise of outstanding options, at a weighted average exercise price of $10.82 per share; and

- 3,538,114 shares of our common stock available for future issuance pursuant to our existing stock incentive plans.

To the extent that outstanding options are exercised or new stock awards are issued under our existing stock incentive plans, investors purchasing our common stock in this offering will experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

Table of Contents

PRICE RANGE OF COMMON STOCK

Our common stock is quoted on The NASDAQ Global Select Market under the symbol PGNX . The following table sets forth, for the periods indicated, the high and low sales price per share of the common stock, as reported on The NASDAQ Global Select Market.

PERIOD	HIGH	LOW
Year Ended December 31, 2014		
First Quarter (January 2 to February 20, 2014)	$ 7.45	4.26
Year Ended December 31, 2013		
First Quarter	5.69	2.53
Second Quarter	5.57	3.54
Third Quarter	6.47	4.36
Fourth Quarter	5.90	3.45
Year Ended December 31, 2012		
First Quarter	10.50	8.32
Second Quarter	11.34	7.44
Third Quarter	11.00	2.81
Fourth Quarter	3.30	1.41
Year Ended December 31, 2011		
First Quarter	6.50	5.32
Second Quarter	8.69	5.97
Third Quarter	7.93	4.50
Fourth Quarter	9.19	5.01

On February 20, 2014, the last sale price of our common stock, as reported on The NASDAQ Global Select Market, was $4.90. There were approximately 88 holders of record of our common stock as of that date.

Table of Contents

DIVIDENDS

We have not paid any dividends since the Company s inception and currently anticipate that all earnings, if any, will be retained for development of our business and that no dividends on our common stock will be declared in the foreseeable future.

Table of Contents

MATERIAL U.S. FEDERAL INCOME AND ESTATE TAX CONSEQUENCES TO NON-U.S. HOLDERS

The following summary describes the material U.S. federal income and estate tax consequences of the acquisition, ownership and disposition of our common stock acquired in this offering by a Non-U.S. Holder (as defined below). This discussion does not address all aspects of U.S. federal income and estate taxes, does not discuss any other U.S. federal tax consequences, and does not deal with foreign, state and local consequences that may be relevant to Non-U.S. Holders in light of their particular circumstances. Special rules may apply to certain Non-U.S. Holders that are subject to special treatment under the U.S. Internal Revenue Code of 1986, as amended (the Code), such as financial institutions, insurance companies, tax-exempt organizations, broker-dealers and traders in securities, U.S. expatriates, controlled foreign corporations, passive foreign investment companies, corporations that accumulate earnings to avoid U.S. federal income tax, persons that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or integrated investment or other risk reduction strategy, partnerships and other pass-through entities, and investors in such pass-through entities. Such Non-U.S. Holders are urged to consult their own tax advisors to determine the U.S. federal, state, local and other tax consequences that may be relevant to them. Furthermore, the discussion below is based upon the provisions of the Code, and Treasury regulations, rulings and judicial decisions thereunder as of the date hereof, and such authorities may be repealed, revoked or modified, perhaps retroactively, so as to result in U.S. federal income and estate tax consequences different from those discussed below. We have not requested a ruling from the U.S. Internal Revenue Service (IRS) with respect to the statements made and the conclusions reached in the following summary, and there can be no assurance that the IRS will agree with such statements and conclusions. This discussion is limited to Non-U.S. Holders that purchase our common stock pursuant to this offering and hold our common stock as a capital asset within the meaning of Code Section 1221 (generally, property held for investment).

The following discussion is for general information only and is not tax advice. Persons considering the purchase of our common stock should consult their own tax advisors concerning the U.S. federal income and estate tax consequences of acquiring, owning and disposing of our common stock in light of their particular situations as well as any consequences arising under the laws of any other taxing jurisdiction, including any state, local or foreign tax consequences, and those arising under any applicable tax treaty.

Except as otherwise described in the discussion of estate tax below, a Non-U.S. Holder is a beneficial owner of our common stock that is not a U.S. Holder or a partnership or other entity treated as a partnership for U.S. tax purposes. A U.S. Holder means a beneficial owner of our common stock that is for U.S. federal income tax purposes (i) an individual who is a citizen or resident of the United States, (ii) a corporation or other entity treated as a corporation created or organized in or under the laws of the United States or any political subdivision thereof, (iii) an estate the income of which is subject to U.S. federal income taxation regardless of its source or (iv) a trust if it (x) is subject to the primary supervision of a court within the United States and one or more U.S. persons have the authority to control all substantial decisions of the trust or (y) has a valid election in effect under applicable U.S. Treasury regulations to be treated as a U.S. person.

If a partnership (including any entity or arrangement treated as a partnership for U.S. federal income tax purposes) acquires our common stock, the tax treatment of a partner in the partnership will generally depend upon the status of the partner and the activities of the partnership. Persons who are partners of partnerships holding our common stock are urged to consult their tax advisors.

Distributions

Subject to the discussion below, distributions, if any, made to a Non-U.S. Holder of our common stock out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles) generally will

constitute dividends for U.S. tax purposes and will be subject to withholding tax at a thirty percent rate or such lower rate as may be specified by an applicable income tax treaty. To obtain a reduced rate of withholding under a treaty, a Non-U.S. Holder generally will be required to provide us with a properly-executed IRS Form W-8BEN, or other appropriate form, certifying the Non-U.S. Holder s entitlement to benefits under that treaty. Treasury regulations provide special rules to determine whether, for purposes of determining the applicability of a tax treaty, dividends paid to a Non-U.S. Holder that is an entity should be treated as paid to the entity or to those holding an interest in

Table of Contents

that entity. If a Non-U.S. Holder holds our common stock through a financial institution or other agent acting on the holder s behalf, the holder will be required to provide appropriate documentation to such agent. The holder s agent will then be required to provide certification to us or our paying agent, either directly or through other intermediaries.

We generally are not required to withhold tax on dividends paid to a Non-U.S. Holder that are effectively connected with the Non-U.S. Holder s conduct of a trade or business within the United States (and, if required by an applicable tax treaty, are attributable to a permanent establishment maintained by the holder in the United States) if a properly-executed IRS Form W-8ECI, stating that the dividends are so connected (and are not exempt from U.S. federal income tax on net income under a treaty as described below), is filed with us. In general, effectively connected dividends will be subject to U.S. federal income tax on net income, generally in the same manner and at the regular rate as if the Non-U.S. Holder were a U.S. citizen or resident alien or a domestic corporation, as the case may be, unless a specific treaty exemption applies. A corporate Non-U.S. Holder receiving effectively connected dividends may also be subject to an additional branch profits tax, which is imposed, under certain circumstances, at a rate of thirty percent (or such lower rate as may be specified by an applicable treaty) of the corporate Non-U.S. Holder s effectively connected earnings and profits, subject to certain adjustments.

If you are eligible for a reduced rate of withholding tax pursuant to a tax treaty, you may generally obtain a refund of any excess amounts currently withheld if you timely file an appropriate claim for refund with the IRS.

To the extent distributions on our common stock, if any, exceed our current and accumulated earnings and profits, they will constitute a return of capital and will first reduce your basis in our common stock, but not below zero, and then will be treated as gain from the sale of stock.

Gain on Disposition of Common Stock

Subject to the discussion below regarding backup withholding and legislation relating to foreign accounts, a Non-U.S. Holder generally will not be subject to U.S. federal income tax with respect to gain realized on a sale or other disposition of our common stock unless (i) the gain is effectively connected with a trade or business of such holder in the United States and, if required by an applicable income tax treaty, attributable to a permanent establishment maintained in the United States by the Non-U.S. Holder, (ii) the Non-U.S. Holder is a nonresident alien individual and is present in the United States for 183 or more days in the taxable year of the disposition and certain other conditions are met, or (iii) we are or have been a United States real property holding corporation within the meaning of Code Section 897(c)(2) at any time within the shorter of the five-year period preceding such disposition or such holder s holding period. In general, we would be a United States real property holding corporation if the fair market value of our interests in U.S. real estate comprised at least half of the sum of the fair market value of worldwide real property interests plus our other assets used or held for use in trade or business. We believe that we are not, and do not anticipate becoming, a United States real property holding corporation. Even if we are treated as a United States real property holding corporation, gain realized by a Non-U.S. Holder on a disposition of our common stock will not be subject to U.S. federal income tax so long as (1) the Non-U.S. Holder owned directly, indirectly and constructively, no more than five percent of our common stock at all times within the shorter of (a) the five year period preceding the disposition or (b) the holder s holding period and (2) our common stock is regularly traded on an established securities market. There can be no assurance that our common stock will continue to qualify as regularly traded on an established securities market.

If you are a Non-U.S. Holder described in (i) above, you will be required to pay tax on the net gain derived from the sale at generally applicable United States federal income tax rates, subject to an applicable income tax treaty providing otherwise, and corporate Non-U.S. Holders described in (i) above may be subject to the branch profits tax at a thirty percent rate or such lower rate as may be specified by an applicable income tax treaty. If you are an individual

Non-U.S. Holder described in (ii) above, you will be required to pay a flat thirty percent tax (or a reduced rate under an applicable income tax treaty) on the gain derived from the sale, which gain may be offset by U.S. source capital losses if you have timely filed tax returns with respect to such losses (even though you are not considered a resident of the United States). If you are a Non-U.S. Holder described in (iii) above and an exception from U.S. federal income tax does not apply (e.g., because our common stock does not qualify as regularly traded on an established securities market or, if it does so qualify, you own more than five percent of our common stock during the relevant period), any gain derived from the sale would be treated as effectively connected with a trade or

Table of Contents

business in the United States, generally taxable in the manner described in (i) above (except that corporate Non-U.S. Holders would not be subject to branch profits tax on such gain), and a withholding tax could apply.

Medicare Contributions Tax

For taxable years beginning after December 31, 2012, a 3.8% Medicare tax will apply, in addition to regular income tax, to certain net investment income (which includes dividends and gains recognized upon a disposition of stock). The 3.8% tax generally applies only to certain U.S. persons with adjusted gross income in excess of certain thresholds. However, the IRS has indicated in proposed Treasury regulations that the 3.8% Medicare tax may be applicable to non-U.S. Holders that are estates or trusts and have one or more U.S. beneficiaries. Non-U.S. Holders that are estates or trusts should consult their tax advisors about the possible application of the 3.8% Medicare tax to any distributions on, or gain realized upon a sale or other disposition of our common stock.

Information Reporting and Backup Withholding

Generally, we must report to the IRS the amount of dividends paid, the name and address of the recipient, and the amount, if any, of tax withheld. A similar report is sent to the holder. Pursuant to tax treaties or certain other agreements, the IRS may make its reports available to tax authorities in the recipient s country of residence. Backup withholding will generally not apply to payments of dividends made by us or our paying agents to a Non-U.S. Holder if the holder provides a valid IRS Form W-8BEN or an acceptable substitute form upon which the holder certifies, under penalties of perjury, that it is not a U.S. person or other documentation upon which the payer may rely to treat the payments as made to a non-U.S. person in accordance with Treasury regulations and the payer otherwise has no knowledge or reason to know that the payee is a U.S. person, or the Non-U.S. Holder otherwise establishes an exemption. The backup withholding rate is currently 28%.

Under current U.S. federal income tax law, information reporting and backup withholding will apply to the proceeds of a disposition of our common stock effected by or through a U.S. office of a broker unless the disposing holder certifies as to its non-U.S. status or otherwise establishes an exemption. Generally, U.S. information reporting and backup withholding will not apply to a payment of disposition proceeds where the transaction is effected outside the United States through a non-U.S. office of a non-U.S. broker. However, information reporting and backup withholding will apply to a payment of disposition proceeds if the broker has actual knowledge or reason to know that the holder is a U.S. person.

Backup withholding is not an additional tax. Rather, the tax liability of persons subject to backup withholding will be reduced by the amount of tax withheld. If withholding results in an overpayment of taxes, a refund may be obtained, provided that the required information is timely furnished to the IRS.

Legislation Relating to Foreign Accounts

Recently enacted legislation may impose withholding tax on certain types of payments made to foreign financial institutions (as specially defined for the purposes of these rules) and certain other non-U.S. entities, unless additional certification, information reporting and other specified requirements are met. The legislation generally imposes a 30% withholding tax on dividends on, and the gross proceeds of a sale or other disposition of, common stock paid to a foreign financial institution or to a non-financial foreign entity, unless (i) the foreign financial institution undertakes certain diligence and reporting obligations or (ii) the non-financial foreign entity either certifies that it does not have any substantial United States owners or provides the name, address and taxpayer identification number of each substantial United States owner and such entity meets certain other specified requirements. If the payee is a foreign financial institution, it must enter into an agreement with the United States Treasury requiring, among other things,

that it undertake to identify accounts held by certain U.S. persons or U.S. owned foreign entities, annually report certain information about such accounts and withhold 30% on payments to account holders whose actions prevent it from complying with these reporting and other requirements. Under certain circumstances, a non-U.S. Holder might be eligible for refunds or credits of such taxes. This new withholding tax will generally not apply to payments of dividends made on or before June 30, 2014, or to payments of gross proceeds from sales or other dispositions of common stock made on or before December 31, 2016. Non-U.S. holders are urged to consult their tax advisors regarding the possible implications of this legislation on their investment in our common stock.

Table of Contents

Federal Estate Tax

An individual who at the time of death is not a citizen or resident of the United States and who is treated as the owner of, or has made certain lifetime transfers of, an interest in our common stock will be required to include the value thereof in his or her taxable estate for U.S. federal estate tax purposes, and may be subject to U.S. federal estate tax unless an applicable estate tax treaty provides otherwise. The test for whether an individual is a resident of the United States for federal estate tax purposes differs from the test used for U.S. federal income tax purposes. Some individuals, therefore, may be Non-U.S. Holders for U.S. federal income tax purposes, but not for U.S. federal estate tax purposes, and vice versa.

THE FOREGOING DISCUSSION OF U.S. FEDERAL INCOME AND ESTATE TAX CONSIDERATIONS IS FOR GENERAL INFORMATION ONLY. IT IS NOT TAX ADVICE. EACH PROSPECTIVE INVESTOR SHOULD CONSULT HIS, HER OR ITS OWN TAX ADVISOR REGARDING THE TAX CONSEQUENCES OF PURCHASING, HOLDING AND DISPOSING OF OUR COMMON STOCK, INCLUDING THE CONSEQUENCES OF ANY PROPOSED CHANGE IN APPLICABLE LAW.

Table of Contents

UNDERWRITING

Subject to the terms and conditions set forth in the underwriting agreement dated as of February 21, 2014, between us and Jefferies LLC, as representative of the underwriters named below and the sole book-running manager of this offering, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the number of shares of common stock shown opposite its name below:

UNDERWRITER	NUMBER OF SHARES
Jefferies LLC	6,086,957
Needham & Company, LLC	798,913
Brean Capital, LLC	722,826
Total	7,608,696

The underwriting agreement provides that the obligations of the underwriters are subject to certain conditions precedent such as the receipt by the underwriters of officers certificates and legal opinions and approval of certain legal matters by their counsel. The underwriting agreement provides that the underwriters will purchase all of the shares, other than those shares covered by the option to purchase additional shares described below, if any of them are purchased. We have agreed to indemnify the underwriters and certain of their controlling persons against certain liabilities, including liabilities under the Securities Act, and to contribute to payments that the underwriters may be required to make in respect of those liabilities.

The underwriters have advised us that, following the completion of this offering, they currently intend to make a market in our common stock as permitted by applicable laws and regulations. The underwriters are not obligated to do so and may discontinue any market-making activities at any time without notice in their sole discretion. Accordingly, no assurance can be given as to the liquidity of the trading market for our common stock that you will be able to sell any of our common stock held by you at a particular time or that the prices that you receive when you sell will be favorable.

The underwriters are offering the shares of our common stock subject to their acceptance of the shares from us and subject to prior sale. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part. In addition, the underwriters have advised us that they do not intend to confirm sales to any account over which they exercise discretionary authority.

Commission and Expenses

The underwriters have advised us that they propose to offer the shares of our common stock to the public at the public offering price set forth on the cover page of this prospectus supplement and to certain dealers at that price less a

concession not in excess of $0.1656 per share of common stock. After the offering, the public offering price, concession and reallowance to dealers may be reduced by the underwriters. No such reduction will change the amount of proceeds to be received by us as set forth on the cover page of this prospectus supplement.

The following table shows the public offering price, the underwriting discounts and commissions that we are to pay the underwriters and the proceeds, before expenses, to us in connection with this offering. Such amounts are shown assuming both no exercise and full exercise of the underwriters option to purchase additional shares.

	PER SHARE		TOTAL	
	WITHOUT OPTION TO PURCHASE ADDITIONAL SHARES	WITH OPTION TO PURCHASE ADDITIONAL SHARES	WITHOUT OPTION TO PURCHASE ADDITIONAL SHARES	WITH OPTION TO PURCHASE ADDITIONAL SHARES
Public offering price	$ 4.600	$ 4.600	$ 35,000,001.60	$ 40,250,000.00
Underwriting discounts and commissions payable by us	$ 0.276	$ 0.276	$ 2,100,000.10	$ 2,415,000.00
Proceeds to us, before expenses	$ 4.324	$ 4.324	$ 32,900,001.50	$ 37,835,000.00

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately $300,000.

Table of Contents

Listing

Our common stock is listed on The NASDAQ Global Select Market under the trading symbol PGNX.

Option to Purchase Additional Shares

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus supplement, to purchase up to an aggregate of 1,141,304 additional shares of our common stock at the public offering price set forth on the cover page of this prospectus supplement, less underwriting discounts and commissions.

No Sales of Similar Securities

We, our executive officers and our directors have agreed, subject to specified exceptions, not to directly or indirectly:

- sell, offer, contract or grant any option to sell (including any short sale), pledge, transfer, establish an open put equivalent position within the meaning of Rule 16a-l(h) under the U.S. Securities Exchange Act of 1934, as amended, or

- otherwise dispose of any shares of our common stock, options or warrants to acquire shares of our common stock, or securities exchangeable or exercisable for or convertible into shares of our common stock currently or hereafter owned either of record or beneficially, or

- publicly announce an intention to do any of the foregoing for a period of 90 days after the date of this prospectus supplement without the prior written consent of the underwriters.

These restrictions terminate after the close of trading of the shares of our common stock on and including the 90th day after the date of this prospectus supplement. However, subject to certain exceptions, in the event that either:

- during the last 17 days of the 90-day restricted period, we issue an earnings release or material news or a material event relating to us occurs, or

- prior to the expiration of the 90-day restricted period, we announce that we will release earnings results during the 16-day period beginning on the last day of the 90-day restricted period,

then in each case the 90-day restricted period will be extended until the expiration of the 18-day period beginning on the date of the issuance of the earnings release or the occurrence of the material news or event, as applicable, unless the underwriters waive, in writing, such extension.

The underwriters may, in their sole discretion and at any time or from time to time before the termination of the 90-day period, without public notice, release all or any portion of the securities subject to lock-up agreements. Other than the exceptions specified in the lock-up agreements, there are no existing agreements between the underwriters and us or any of our stockholders who will execute a lock-up agreement providing consent to the sale of shares prior to the expiration of the restricted period.

Stabilization

The underwriters have advised us that, pursuant to Regulation M under the Exchange Act, certain persons participating in the offering may engage in short sale transactions, stabilizing transactions, syndicate covering transactions or the imposition of penalty bids in connection with this offering. These activities may have the effect of stabilizing or maintaining the market price of our common stock at a level above that which might otherwise prevail in the open market. Establishing short sales positions may involve either covered short sales or naked short sales.

Covered short sales are sales made in an amount not greater than the underwriters option to purchase additional shares of our common stock in this offering. The underwriters may close out any covered short position by either exercising their option to purchase additional shares of our common stock or purchasing shares of our common stock in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option to purchase additional shares.

Naked short sales are sales in excess of the option to purchase additional shares of our common stock. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of our common stock in the open market after pricing that could adversely affect investors who purchase in this offering.

Table of Contents

A stabilizing bid is a bid for the purchase of shares of our common stock on behalf of the underwriters for the purpose of fixing or maintaining the price of our common stock. A syndicate covering transaction is the bid for or the purchase of shares of our common stock on behalf of the underwriters to reduce a short position incurred by the underwriters in connection with the offering. Similar to other purchase transactions, the underwriters purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. A penalty bid is an arrangement permitting the underwriters to reclaim the selling concession otherwise accruing to a syndicate member in connection with the offering if shares of our common stock originally sold by such syndicate member are purchased in a syndicate covering transaction and therefore have not been effectively placed by such syndicate member.

Neither we nor the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. The underwriters are not obligated to engage in these activities and, if commenced, any of the activities may be discontinued at any time.

The underwriters may also engage in passive market making transactions in our common stock on The NASDAQ Global Market in accordance with Rule 103 of Regulation M during a period before the commencement of offers or sales of shares of our common stock in this offering and extending through the completion of distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker s bid, that bid must then be lowered when specified purchase limits are exceeded.

Electronic Distribution

A prospectus in electronic format may be made available by e-mail or on web sites or through online services maintained by the underwriters or their affiliates. In those cases, prospective investors may view offering terms online and may be allowed to place orders online. The underwriters may agree with us to allocate a specific number of shares of our common stock for sale to online brokerage account holders. Any such allocation for online distributions will be made by the underwriters on the same basis as other allocations. Other than the prospectus in electronic format, the information on the underwriters web sites and any information contained in any other web site maintained by any of the underwriters is not part of this prospectus supplement, has not been approved and/or endorsed by us or the underwriters and should not be relied upon by investors.

Other Activities and Relationships

The underwriters and certain of their affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. The underwriters and certain of their affiliates may in the future perform, various financial advisory and investment banking services for the issuer, for which they received or will receive customary fees and expenses.

In the ordinary course of their various business activities, the underwriters and certain of their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers, and such investment and securities activities may involve securities and/or instruments of the issuer. The underwriters and certain of their affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Table of Contents

NOTICE TO INVESTORS

European Economic Area

In relation to each member state of the European Economic Area which has implemented the Prospectus Directive (each, a Relevant Member State), an offer to the public of any shares of our common stock which are the subject of the offering contemplated by this prospectus supplement and the accompanying prospectus may not be made in that Relevant Member State except that an offer to the public in that Relevant Member State of any shares of our common stock may be made at any time under the following exemptions under the Prospectus Directive, if they have been implemented in that Relevant Member State:

(a) to any legal entity which is a qualified investor as defined in the Prospectus Directive;

(b) to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the underwriters nominated by us for any such offer; or

(c) in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of shares of our common stock shall require us or the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

For the purposes of this provision, the expression an offer of shares of our common stock to the public in relation to the shares of our common stock in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the shares of our common stock to be offered so as to enable an investor to decide to purchase or subscribe to the shares of our common stock, as the same may be varied in that Relevant Member State by any measure implementing the Prospectus Directive in that Relevant Member State and the expression Prospectus Directive means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State), and includes any relevant implementing measure in the Relevant Member State and the expression 2010 PD Amending Directive means Directive 2010/73/EU.

Switzerland

The securities may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange (SIX) or on any other stock exchange or regulated trading facility in Switzerland. This prospectus supplement and the accompanying prospectus has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this prospectus supplement nor any other offering or marketing material relating to the securities or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this Offering Memorandum nor any accompanying prospectus nor any other offering or marketing material relating to the offering, the Company or the securities have been or will be filed with or approved by any Swiss regulatory authority. In particular, this this prospectus supplement and the accompanying prospectus will not be filed with, and the offer of securities will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA

(FINMA), and the offer of securities has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes (CISA). The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of securities.

Table of Contents

United Kingdom

This prospectus supplement and the accompanying prospectus is only being distributed to, and is only directed at, persons in the United Kingdom that are qualified investors within the meaning of Article 2(1)(e) of the Prospectus Directive that are also (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (Order) and/or (ii) high net worth entities falling within Article 49(2)(a) to (d) of the Order and other persons to whom it may lawfully be communicated (each such person being referred to as a relevant person).

This prospectus supplement and the accompanying prospectus and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other persons in the United Kingdom. Any person in the United Kingdom that is not a relevant person should not act or rely on this document or any of its contents.

Italy

This prospectus supplement and the accompanying prospectus have not been and will not be filed with or cleared by the Italian securities exchange commission, Commissione Nazionale per le societa e la Borsa (CONSOB), pursuant to Legislative Decree No. 58 of 24 February 1998, as amended (Finance Law), and to CONSOB Regulation No. 11971 of 14 May 1999, as amended (Issuers Regulation). Accordingly, copies of this prospectus supplement and the accompanying prospectus or any other document relating to our common stock may not be distributed, made available or advertised in Italy, nor may our common stock be offered, purchased, sold, promoted, advertised or delivered, directly or indirectly, to the public other than (i) to Professional Investors (such being the persons and entities as defined pursuant to article 31(2) of CONSOB Regulation No. 11522 of 1 July 1998, as amended, the Intermediaries Regulation) pursuant to article 100 of the Finance Law; (ii) to prospective investors where the offer of our common stock relies on the exemption from the investment solicitation rules pursuant to, and in compliance with, the conditions set out by article 100 of the Finance Law and article 33 of the Issuers Regulation, or by any applicable exemption; provided that any such offer, sale, promotion, advertising or delivery of our common stock or distribution of this prospectus supplement and the accompanying prospectus, or any part thereof, or of any other document or material relating to our common stock in Italy is made: (a) by investment firms, banks or financial intermediaries authorized to carry out such activities in the Republic of Italy in accordance with the Finance Law, the Issuers Regulation, Legislative Decree No. 385 of 1 September 1993, as amended (Banking Law), the Intermediaries Regulation, and any other applicable laws and regulations; and (b) in compliance with any applicable notification requirement or duty which may, from time to time, be imposed by CONSOB, Bank of Italy or by any other competent authority.

Germany

Any offer or solicitation of securities within Germany must be in full compliance with the German Securities Prospectus Act (Wertpapierprospektgesetz WpPG). The offer and solicitation of securities to the public in Germany requires the publication of a prospectus that has to be filed with and approved by the German Federal Financial Services Supervisory Authority (Bundesanstalt für Finanzdienstleistungsaufsicht BaFin). This prospectus supplement and the accompanying prospectus have not been and will not be submitted for filing and approval to the BaFin and, consequently, will not be published. Therefore, this prospectus supplement does not constitute a public offer under the German Securities Prospectus Act (Wertpapierprospektgesetz). This prospectus supplement, the accompanying prospectus and any other document relating to our common stock, as well as any information contained therein, must therefore not be supplied to the public in Germany or used in connection with any offer for subscription of our common stock to the public in Germany, any public marketing of our common stock or any public solicitation for

offers to subscribe for or otherwise acquire our common stock. This prospectus supplement, the accompanying prospectus and other offering materials relating to the offer of our common stock are strictly confidential and may not be distributed to any person or entity other than the designated recipients hereof.

Table of Contents

France

This prospectus supplement and the accompanying prospectus have not been prepared in the context of a public offering of financial securities in France within the meaning of Article L.411-1 of the French Code Monétaire et Financier and Title I of Book II of the Règlement Général of the Autorité des marchés financiers (the AMF) and therefore has not been and will not be filed with the AMF for prior approval or submitted for clearance to the AMF. Consequently, the shares of our common stock may not be, directly or indirectly, offered or sold to the public in France and offers and sales of the shares of our common stock may only be made in France to qualified investors (investisseurs qualifiés) acting for their own, as defined in and in accordance with Articles L.411-2 and D.411-1 to D.411-4, D.734-1, D.744-1, D.754-1 and D.764-1 of the French Code Monétaire et Financier. None of this prospectus supplement, the accompanying prospectus or any other offering material may be released, issued or distributed to the public in France or used in connection with any offer for subscription on sale of the shares of our common stock to the public in France. The subsequent direct or indirect retransfer of the shares of our common stock to the public in France may only be made in compliance with Articles L.411-1, L.411-2, L.412-1 and L.621-8 through L.621-8-3 of the French Code Monétaire et Financier.

Sweden

This is not a prospectus under, and has not been prepared in accordance with the prospectus requirements provided for in, the Swedish Financial Instruments Trading Act [lagen (1991:980) om handel med finasiella instrument] nor any other Swedish enactment. Neither the Swedish Financial Supervisory Authority nor any other Swedish public body has examined, approved, or registered this document.

Table of Contents

LEGAL MATTERS

The validity of the common stock offered by this prospectus supplement and the accompanying prospectus will be passed upon for us by O Melveny & Myers LLP, Menlo Park, California. Wilmer Cutler Pickering Hale and Dorr LLP, New York, New York, is counsel for the underwriters in connection with this offering.

Table of Contents

EXPERTS

The financial statements as of December 31, 2011 and for the two years ended December 31, 2011 incorporated in this prospectus supplement and the accompanying prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2012 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

The financial statements and management s assessment of the effectiveness of internal control over financial reporting (which is included in Management s Report on Internal Control over Financial Reporting) incorporated in this prospectus supplement and the accompanying prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2012 have been so incorporated in reliance on the report of Ernst & Young LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

The consolidated financial statements of Molecular Insight Pharmaceuticals, Inc. as of December 31, 2012 and 2011 (Successor), and for the year ended December 31, 2012 (Successor) and the consolidated statements of operations, stockholders equity (deficit), and cash flows for the period from June 1, 2011 to December 31, 2011 (Successor), and for the period January 1, 2011 to May 31, 2011 (Predecessor) all incorporated by reference in this prospectus supplement and in the Registration Statement have been so incorporated in reliance on the report of BDO USA, LLP, a certified public accounting firm, appearing elsewhere herein and in the Registration Statement given on the authority of said firm as experts in auditing and accounting.

Table of Contents

WHERE YOU CAN FIND MORE INFORMATION

This prospectus supplement and the accompanying prospectus are part of a registration statement on Form S-3 that we filed with the SEC under the Securities Act on January 23, 2014, which registration statement was declared effective by the SEC on February 5, 2014. This prospectus supplement and the accompanying prospectus, which constitute a part of the registration statement, do not contain all the information set forth in the registration statement and the exhibits to the registration statement or the exhibits to the reports or other documents incorporated by reference in this prospectus supplement and the accompanying prospectus. For further information about us, the common stock we are offering by this prospectus supplement and the accompanying prospectus and related matters, you should review the registration statement, including the exhibits filed as a part of the registration statement and the exhibits to the reports or other documents incorporated by reference in this prospectus supplement and the accompanying prospectus. Whenever a reference is made in this prospectus supplement or the accompanying prospectus to any of our contracts, agreements or other documents, the reference may not be complete and you should refer to the exhibits that are a part of the registration statement or the exhibits to the reports or other documents incorporated by reference in this prospectus supplement and the accompanying prospectus for a copy of such contract, agreement or other document.

Because we are subject to the information and periodic reporting requirements of the Exchange Act, we file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings and the registration statement of which this prospectus supplement and the accompanying prospectus are a part, as well as the exhibits that were filed with the registration statement and the exhibits to the reports or other documents incorporated by reference in this prospectus supplement and the accompanying prospectus, are available to the public over the Internet at the SEC s website at www.sec.gov. You may also read and copy any document we file at the SEC s Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Information on the operation of the public reference facilities may be obtained by calling the SEC at 1-800-SEC-0330. You may also request copies of these filings, at no cost, by telephone at (914) 789-2800 or by mail to: Progenics Pharmaceuticals, Inc., 777 Old Saw Mill River Road, Tarrytown, New York 10591, Attention: Investor Relations and Corporate Communications.

We maintain a website at www.progenics.com, which contains information about Progenics, Molecular Insight and our other subsidiaries and at which you may access our periodic reports and other information filed or furnished by us with the SEC free of charge. The information contained on, or that can be accessed through, our website is not incorporated by reference in this prospectus supplement and the accompanying prospectus and you should not consider it a part of this prospectus supplement and the accompanying prospectus.

Table of Contents

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

SEC rules permit us to incorporate by reference information in this prospectus supplement and the accompanying prospectus. This 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 considered to be part of this prospectus supplement and the accompanying prospectus, except for information superseded by information contained in this prospectus supplement or the accompanying prospectus itself or in any subsequently filed incorporated document. Any statement contained herein or in a document incorporated or deemed to be incorporated by reference in this prospectus supplement or the accompanying prospectus shall be deemed to be modified or superseded for purposes of this prospectus supplement and the accompanying prospectus to the extent that a statement contained in this prospectus supplement or the accompanying prospectus, or in any other subsequently filed document which also is or is deemed to be incorporated by reference in this prospectus supplement or the accompanying prospectus, modifies or supersedes such earlier statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus supplement and the accompanying prospectus.

We incorporate by reference in this prospectus supplement and the accompanying prospectus the documents listed below and any future documents we file with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus supplement and until the completion or termination of this offering (in each case, except for the information in any of the foregoing Current Reports on Form 8-K furnished under Item 2.02 or Item 7.01 thereof). These documents contain important information about Progenics and its business and financial condition:

- our Annual Report on Form 10-K for the year ended December 31, 2012, as amended by Amendments Nos. 1 and 2 thereto on Form 10-K/A;

- our Quarterly Reports on Form 10-Q for the periods ended March 31, June 30 and September 30, 2013;

- our Current Reports on Form 8-K filed on January 22, 2013 (as amended by Amendments Nos. 1, 2 and 3 on Form 8-K/A filed on April 4 and June 19, 2013 and February 20, 2014, respectively); February 14, 2013; March 5, 2013; May 17, 2013; June 3, 4, 5, 10, 11, 13, 17, 21 and 25, 2013; July 1, 2013; July 16, 2013 (two filings); August 9, 2013; September 12, 2013; October 2 and 22, 2013; November 12 and 25, 2013; December 9, 2013; January 24, 2014; January 29, 2014 (two filings); January 30, 2014; and February 6, 2014 (two filings); and

- the description of our common stock contained in our registration statement on Form 8-A, dated September 29, 1997, including any amendments or reports filed for the purpose of updating such description.

You may obtain documents incorporated by reference in this prospectus supplement and the accompanying prospectus by requesting them in writing or by telephone from us at our executive offices at:

Progenics Pharmaceuticals, Inc.

777 Old Saw Mill River Road

Tarrytown, New York 10591

(914) 789-2800

Attention: Investor Relations and Corporate Communications

Table of Contents

PROSPECTUS

$150,000,000

Common Stock, Preferred Stock, Debt Securities, Warrants, Other Rights and/or Units

From time to time, we may sell Common Stock, Preferred Stock, Debt Securities, Warrants, other Rights and/or Units in one or more issuances. This prospectus describes the general manner in which those securities may be offered using this prospectus. We will specify in an accompanying prospectus supplement the terms of securities offered and the offering thereof. Our common stock, currently the only Progenics security outstanding, is listed on The NASDAQ Stock Market LLC under the symbol PGNX.

Investing in our securities involves a high degree of risk. See Risk Factors and Forward-Looking Statements on page 8 & 4.

The securities covered by this prospectus may be sold directly by us to investors, through agents designated from time to time or through underwriters or dealers at prices and on terms to be determined at the time of offering. We will include in the accompanying prospectus supplement the names of any underwriters or agents and any applicable commissions or discounts; additional information on the methods of sale appears under Plan of Distribution. We will also describe in the prospectus supplement the way(s) in which we expect to use the net proceeds we receive from any sale.

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

This prospectus may not be used to offer or sell any securities unless accompanied by a prospectus supplement.

The date of this prospectus is February 5, 2014.

Table of Contents

TABLE OF CONTENTS

You should rely only on the information contained or incorporated by reference in this prospectus and in any applicable supplement to this prospectus. 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 are not making 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 accompanying prospectus supplement and any free writing prospectus prepared by or on behalf of us is accurate only as of the date on their respective covers. Additionally, any information we have incorporated by reference in this prospectus or in any applicable prospectus supplement is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus, any applicable prospectus supplement or any sale of securities. Our business, financial condition, results of operations and prospects may have changed since that date.

This prospectus and any applicable prospectus supplement contain and incorporate by reference market data, industry statistics and other data that have been obtained or compiled from information made available by third parties. We have not independently verified such data. This prospectus, any applicable prospectus supplement and the information incorporated herein or therein by reference include trademarks, service marks and trade names owned by us or other companies. All trademarks, service marks and trade names included or incorporated by reference in this prospectus, any applicable prospectus supplement or any related free writing prospectus are the property of their respective owners.

When used in this prospectus, the terms Progenics, we, our and us refer to Progenics Pharmaceuticals, Inc., a Delaware corporation, and its subsidiaries, unless otherwise specified.

This prospectus, any accompanying prospectus supplement and the information incorporated herein and therein by reference, include trademarks, service marks and trade names owned by us or other companies. All trademarks, service marks and trade names included or incorporated by reference in this prospectus supplement or the accompanying prospectus are the property of their respective owners.

Table of Contents

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that Progenics has filed with the U.S. Securities and Exchange Commission (SEC) using a shelf registration process.

By using a shelf registration statement, we may, from time to time, offer and sell Progenics securities described in this prospectus in one or more offerings with an aggregate total offering price of not more than $150 million. This prospectus describes the general manner in which we may offer Progenics securities by this prospectus. Each time we sell securities pursuant to the registration statement we will provide a prospectus supplement (which term includes, as applicable, the at-the-market sales agreement prospectus filed with the registration statement of which this prospectus forms a part) that will contain specific information about the offering and the securities offered and may also add, update or change information contained in this prospectus. If there is any inconsistency between information in this prospectus and the accompanying prospectus supplement, you should rely on the information in the latest supplement and documents incorporated by reference herein. This prospectus may not be used to offer to sell, solicit an offer to buy or consummate a sale of Progenics securities unless it is accompanied by a prospectus supplement.

This prospectus, together with the accompanying prospectus supplement, contains important information you should know before investing, including important information about Progenics and the securities being offered. You should carefully read both documents, as well as the additional information contained in the documents described under Where You Can Find More Information and Incorporation of Certain Information by Reference in both this prospectus and the accompanying prospectus supplement, and in particular the periodic and current reporting documents we file with the SEC.

Table of Contents

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-3 under the Securities Act of 1933, as amended, with respect to the securities offered by this prospectus and the accompanying prospectus supplement. This prospectus and the accompanying prospectus supplement do not contain all of the information set forth in the registration statement and its exhibits and schedules in accordance with SEC rules and regulations. For further information with respect to Progenics and the securities being offered hereby, you should read the registration statement, including its exhibits and schedules. Statements contained in this prospectus and the accompanying prospectus supplement, including documents that we have incorporated by reference, as to the contents of any contract or other document referred to are not necessarily complete, and, with respect to any contract or other document filed as an exhibit to the registration statement or any other such document, each such statement is qualified in all respects by reference to the corresponding exhibit. You should review the complete document to evaluate these statements. You may obtain copies of the registration statement and its exhibits via the SEC s EDGAR database or our website, or at the offices of the SEC, where they may be examined without charge at the Public Reference Room, at the address listed below, or obtained upon payment of the prescribed fees.

We file annual, quarterly and current reports, proxy statements and other documents with the SEC under the U.S. Securities Exchange Act of 1934, as amended. The SEC maintains a website that contains reports, proxy and information statements and other information regarding issuers, including Progenics, that file electronically with the SEC. You may obtain documents that we file with the SEC at www.sec.gov and read and copy them at the SEC s Public Reference Room at 100 F Street NE, Washington, DC 20549 (information on operation of the Public Reference Room is available by calling the SEC at 1-800-SEC-0330).

We also make these documents available on our website at www.progenics.com. Our website and the information contained or connected to our website is not incorporated by reference in this prospectus or any prospectus supplement, and you should not consider it part of this prospectus or any prospectus supplement.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

SEC rules permit us to incorporate by reference information in this prospectus and the accompanying prospectus supplement. This 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 considered to be part of this prospectus and the accompanying prospectus supplement, except for information superseded by information contained in this prospectus and/or the accompanying prospectus supplement itself or in any subsequently filed incorporated document. This prospectus and the accompanying prospectus supplement incorporate by reference the documents set forth below that we have previously filed with the SEC (Commission File No. 0-23143), other than information in such documents that is deemed to be furnished and not filed. These documents contain important information about Progenics and its business and financial condition.

Annual Report on Form 10-K for the year ended December 31, 2012, as amended by Amendments No. 1 and 2 to the Annual Report on Form 10-K/A;

Quarterly Reports on Form 10-Q for the periods ended March 31, June 30 and September 30, 2013;

Current Reports on Form 8-K filed on January 22 (as amended by Amendments No. 1 and 2 on Form 8-K/A filed on April 4 and June 19, respectively); February 14; March 5; May 17; June 3, 4, 5, 10, 11, 13, 17, 19, 21 and 25; July 1 and 16 (two filings); August 9; September 12; October 2 and 22; November 12 and 25; and December 9, 2013; and

the description of our common stock contained in our Registration Statement on Form 8-A, dated September 29, 1997, including any amendments or reports filed for the purpose of updating such description.

Table of Contents

All documents filed by us pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act subsequent to the date of this prospectus and prior to the completion of this offering and after the date of the initial registration statement and prior to the effectiveness of the registration statement shall be deemed to be incorporated by reference in this prospectus and the accompanying prospectus supplement and to be a part hereof from the date of filing of such documents.

Any statement contained herein or in a document incorporated or deemed to be incorporated by reference in this prospectus or the accompanying prospectus supplement shall be deemed to be modified or superseded for purposes of this prospectus and such supplement to the extent that a statement contained in this prospectus or such supplement, or in any other subsequently filed document which also is or is deemed to be incorporated by reference in this prospectus and such supplement, modifies or supersedes such earlier statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus or such supplement.

Documents incorporated by reference are available from us without charge, excluding all exhibits unless specifically incorporated by reference as an exhibit to this prospectus and the accompanying prospectus supplement. Prospective investors may obtain documents incorporated by reference in this prospectus and the accompanying prospectus supplement by requesting them in writing or by telephone from us at our executive offices at:

Progenics Pharmaceuticals, Inc.

777 Old Saw Mill River Road

Tarrytown, New York 10591

(914) 789-2800

Attention: Investor Relations and Corporate Communications

Table of Contents

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

Certain statements contained or incorporated by reference in this prospectus, any accompanying prospectus supplement and any related free writing prospectus constitute forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 and releases issued by the SEC and within the meaning of Section 27A of the Securities Act of 1933, as amended (Securities Act), and Section 21E of the Securities Exchange Act of 1934, as amended (Exchange Act). From time to time, we publish forward-looking statements relating to matters such as anticipated financial performance, business prospects, technological developments, new products, research and development activities and other aspects of our present and future business operations as well as similar matters.

Forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause our or our industry s actual results, levels of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied by such forward-looking statements. While it is impossible to identify or predict all such matters, these differences may result from, among other things, the inherent uncertainty of the timing and success of, and expense associated with, research, development, regulatory approval and commercialization of our products and product candidates, including the risks that clinical trials will not commence or proceed as planned; products appearing promising in early trials will not demonstrate efficacy or safety in larger-scale trials; clinical trial data on our products and product candidates will be unfavorable; our products will not receive marketing approval from regulators or, if approved, do not gain sufficient market acceptance to justify development and commercialization costs; competing products currently on the market or in development might reduce the commercial potential of our products; we, our collaborators or others might identify side effects after the product is on the market; or efficacy or safety concerns regarding marketed products, whether or not originating from subsequent testing or other activities by us, governmental regulators, other entities or organizations or otherwise, and whether or not scientifically justified, may lead to product recalls, withdrawals of marketing approval, reformulation of the product, additional pre-clinical testing or clinical trials, changes in labeling of the product, the need for additional marketing applications, declining sales or other adverse events.

We are also subject to risks and uncertainties associated with the actions of our corporate, academic and other collaborators and government regulatory agencies, including risks from market forces and trends; potential product liability; intellectual property, litigation and other dispute resolution, environmental and other risks; the risk that we may not be able to enter into favorable collaboration or other relationships or that existing or future relationships may not proceed as planned; the risk that current and pending patent protection for our products may be invalid, unenforceable or challenged, or fail to provide adequate market exclusivity, or that our rights to in-licensed intellectual property may be terminated for our failure to satisfy performance milestones; the risk of difficulties in, and regulatory compliance relating to, manufacturing products; and the uncertainty of our future profitability.

Risks and uncertainties also include general economic conditions, including interest and currency exchange-rate fluctuations and the availability of capital; changes in generally accepted accounting principles; the impact of legislation and regulatory compliance; the highly regulated nature of our business, including government cost-containment initiatives and restrictions on third-party payments for our products; trade buying patterns; the competitive climate of our industry; and other factors set forth in this document and other reports filed with the SEC. In particular, we cannot assure you that Relistor® will be commercially successful or be approved in the future in other formulations, indications or jurisdictions, or that any of our other programs will result in a commercial product.

In some cases, you can identify forward-looking statements by terminology such as expect, anticipate, estimate, plan, believe, could, int predict, may, should, will and words of similar import regarding our expectations. Forward-looking statements are only predictions and actual events or results may differ materially. Although we believe that our expectations are based on reasonable assumptions within the bounds of our current knowledge of our industry, business and operations, we cannot guarantee that actual results

Table of Contents

will not differ materially from our expectations. In evaluating such forward-looking statements, you should specifically consider various factors, including the risks outlined under the heading Risk Factors contained in this prospectus, any accompanying prospectus supplement and any related free writing prospectus, and in our most recent Annual Report on Form 10-K and in our most recent Quarterly Report on Form 10-Q, as well as any amendments thereto or Current Reports on Form 8-K filed with the SEC. The discussion of risks and uncertainties set forth in those filings is not necessarily a complete or exhaustive list of all risks facing us at any particular point in time. We operate in a highly competitive, highly regulated and rapidly changing environment, and our business is in a state of evolution. Therefore, it is likely that over time new risks will emerge and the nature and elements of existing risks will change. It is not possible for management to predict all such risk factors or changes therein or to assess either the impact of all such risk factors on our business or the extent to which any individual risk factor, combination of factors or new or altered factors may cause results to differ materially from those contained in any forward-looking statement. Forward-looking statements represent our estimates and assumptions only as of the date such forward-looking statements are made. You should carefully read this prospectus, any accompanying prospectus supplement and any related free writing prospectus, together with the information incorporated herein or therein by reference, and with the understanding that our actual future results may materially differ from what we expect.

Except as required by law, forward-looking statements speak only as of the date they are made. We do not have a policy of updating or revising forward-looking statements and we assume no obligation to update any statements as a result of new information or future events or developments. It should not be assumed that our silence over time means that actual events are bearing out as expressed or implied in forward-looking statements.

Table of Contents

THE COMPANY

This summary contains a general summary of the information contained in this prospectus. It may not include all the information that is important to you. You should read the entire prospectus, any prospectus supplement delivered with the prospectus and the documents incorporated by reference before making an investment decision.

Overview

Progenics develops innovative medicines for oncology. A significant part of our research and development efforts centers on prostate specific membrane antigen (PSMA), a protein found at high levels on the surface of prostate cancer cells and also on the neovasculature of a number of other types of solid tumors. We are conducting phase 2 clinical trials of two product candidates for prostate cancer targeted toward PSMA: our therapeutic candidate, PSMA ADC, a fully human monoclonal antibody-drug conjugate (ADC), and MIP-1404, an imaging agent candidate in development by our Molecular Insight Pharmaceuticals (MIP) subsidiary. PSMA ADC, which utilizes technology licensed to us from Sloan-Kettering Institute for Cancer Research, through Cytogen Corporation, and Seattle Genetics, Inc., is designed to utilize our proprietary fully human monoclonal anti-PSMA antibody to deliver a chemotherapeutic agent to cancer cells by targeting the three-dimensional structure of PSMA. Among other assets in our pipeline of targeted radiotherapy and molecular imaging compounds are a group of small molecule therapeutics, MIP-1095, -1555 and -1558, in preclinical study for metastatic prostate cancer and other PSMA-expressing cancers, and Azedra , an ultra-orphan radiotherapy candidate in a pivotal phase 2 clinical trial for pheochromocytoma.

Progenics has developed internally and acquired from research institutions, pharmaceutical and biotechnology companies certain compounds and technologies which we are advancing with other parties, including our first commercial drug, Relistor® (methylnaltrexone bromide) subcutaneous injection for the treatment of opioid induced constipation (OIC), which we have licensed to Salix Pharmaceuticals, Inc. worldwide other than Japan, where we have licensed the subcutaneous formulation of the drug to Ono Pharmaceutical Co., Ltd. We have suspended investment in our proprietary phosphoinositide 3-kinase (PI3K) inhibitor research and are evaluating alternative paths forward for this program. We continue to consider opportunities for strategic collaborations, out-licenses and other arrangements with biopharmaceutical companies involving our proprietary research, development and clinical programs, and may in the future also in-license or acquire additional oncology compounds and/or programs.

Our current principal sources of revenue from operations are upfront, commercialization milestones, royalty and revenue-sharing payments from Salix s Relistor operations. Royalty and milestone payments from Relistor depend on success in development and commercialization, which is dependent on many factors, such as the actions of Salix and Ono, decisions by the U.S. Food and Drug Administration and other regulatory bodies, the outcome of clinical and other testing of Relistor, and, to the extent requested by our collaboration partners, our own efforts. We and Salix have sought to expand the availability of subcutaneous Relistor to patients taking opioids for non-cancer pain and who suffer from OIC as a result, and to develop an oral formulation of methylnaltrexone for use by such patients. Salix and Progenics have continued to work together with the FDA to generate a reasonable path forward for the further development and regulatory review of Relistor in light of the FDA s complete response action taken in July 2012 regarding Salix s Relistor sNDA for chronic pain, in which the FDA requested additional data. After an End-of-Review meeting in October 2012, the FDA s Division of Gastroenterology and Inborn Errors Products expressed a concern that there may be a risk associated with the chronic use of mu-opioid antagonists in patients who are taking opioids for chronic pain, and, in order to understand this potential risk, the Division communicated that a very large, well-controlled, chronic administration trial will have to be conducted to assess the safety of any mu-opioid antagonist prior to market approval for the treatment of patients with OIC who are taking opioids for chronic, non-cancer pain. Salix subsequently held discussions with the Division and expressed the view that the post-marketing, clinical and preclinical data currently available for Relistor adequately demonstrate an appropriate and expected safety profile

Table of Contents

sufficient to permit the approval of the current Relistor sNDA. In response to Salix s formal appeal of the FDA s complete response letter, the FDA has informed Salix and Progenics that it will seek input from an Advisory Committee, which is expected to convene on March 10-11, 2014. The FDA has also stated that it will take action under the appeal within 30 days after receiving input from the Committee.

Progenics in October 2013 commenced an arbitration with Ono under the provisions of the parties License Agreement, following a communication from Ono that it has determined to discontinue development of subcutaneous Relistor in Japan because of commercial concerns that Ono contends would permit it to cease development and terminate the Agreement. Under our Agreement with Ono, Ono may cease development of subcutaneous Relistor only if it terminates the License Agreement, which it may do unilaterally only if Progenics is in material default. Progenics is not in default under the Agreement, and Ono has neither asserted that Progenics is, nor terminated the Agreement.

Our Corporate Information

Progenics, which has been listed on NASDAQ since 1997, was incorporated in Delaware in 1986, commenced principal operations in 1988, and throughout has been engaged primarily in research and development efforts, establishing corporate collaborations and related activities. Additional information concerning the Company is contained in the documents we file with the SEC, as described above. We maintain a website at www.progenics.com which contains information about Progenics, Molecular Insight and our other subsidiaries. Information contained in or accessed through our website is not part of or incorporated into this prospectus and should not be considered part of any offering documents.

Our mailing address is 777 Old Saw Mill River Road, Tarrytown, New York 10591 (telephone number (914) 789-2800), where our principal executive offices are located and all of our operations are conducted.

Table of Contents

RISK FACTORS

An investment in Progenics securities is speculative in nature and involves a high degree of risk. You should carefully consider the discussion of the material risks of investing in our securities contained in our filings with the SEC, including those identified under Where You Can Find More Information, as well as in any applicable prospectus supplement, in evaluating Progenics and its business and prospects. You should also be aware that this document and other public statements we make may contain statements that do not relate strictly to historical fact, any of which may be forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act of 1995, and should take into account the considerations relating to such statements referred to in Part I, Item 1A of our Annual Report on Form 10-K/A for the fiscal year ended December 31, 2012, filed with the SEC on January 17, 2014, and Part II, Item 1A of our most recent Quarterly Report on Form 10-Q filed with the SEC, and other documents and public statements. Any of the risks and uncertainties set forth therein could materially and adversely affect our business, results of operations and financial condition, which in turn could materially and adversely affect the trading price or value of our securities. As a result, you could lose all or part of your investment.

Table of Contents

USE OF PROCEEDS

Unless we indicate otherwise in an accompanying prospectus supplement, we currently intend to use net proceeds from sales of securities to fund:

- research and development activities, including clinical trials, for product candidates;
- in-licensing of technology, establishment of research and development collaborations, and/or merger or acquisition opportunities; and/or
- working capital and general corporate purposes.

We may set forth additional information concerning our expected use of net proceeds from sales of securities in a prospectus supplement relating to the specific offering. Pending use of net proceeds as described above, we intend to invest net proceeds in interest-bearing, investment-grade securities.

An accompanying prospectus supplement may not identify precisely the amounts we plan to spend on each of the uses of proceeds listed above or any other uses of proceeds that we may identify in the prospectus supplement. In addition, the amounts actually expended for each purpose may vary significantly depending upon numerous factors, including:

- the costs and results of research, development and product candidate testing, including clinical trials;
- costs and results of the regulatory approval process;
- costs and structure of potential acquisitions, collaborations or other transactions;
- the structure of and changes in our relationships with Salix, Ono and other licensors, licensees and collaborators;
- the costs of filing, prosecuting, defending and enforcing patent claims;
- manufacturing, marketing and other costs associated with commercialization of products; and
- changes in the focus and direction of our research and development programs.

DIVIDEND POLICY

We have never declared or paid any cash dividends on our capital stock and do not anticipate paying any cash dividends in the foreseeable future. Payment of cash dividends, if any, in the future will be at the discretion of our board of directors and will depend on then-existing conditions, including our financial condition, operating results, contractual restrictions, capital requirements, business prospects and other factors our board of directors may deem relevant.

9

Table of Contents

RATIO OF EARNINGS (LOSS) TO COMBINED FIXED CHARGES AND PREFERRED STOCK DIVIDENDS

The following table sets forth our ratios of earnings (loss) to combined fixed charges and preferred stock dividends for the periods indicated (in thousands). For these ratios, loss is computed adding loss from operations and fixed charges. Fixed charges consist of an estimate of the interest within rental expense. We do not have any preferred stock outstanding as of the date of this prospectus, and therefore there are no preferred dividends included in our calculation of these ratios.

	Nine Months Ended September 30, 2013	Years Ended December 31, 2012	2011	2010	2009	2008
Ratio of earnings (loss) to fixed charges and preferred stock dividends	*	*	16	*	*	*
Coverage deficiency amount for total fixed charges and preferred stock dividends(1)	$ 34,021	$ 35,431	$	$ 69,820	$ 30,612	$ 44,672

(1) For the years ended 2008 through 2010 and 2012 and for the nine months ended September 30, 2013, the Company s coverage ratio is less than one-to-one and it must generate additional earnings of these specified amounts to achieve a coverage ratio of 1:1.

Table of Contents

GENERAL DESCRIPTION OF SECURITIES

We may offer shares of common and/or preferred stock, various series of debt securities, warrants and/or other rights to purchase securities, and/or units consisting of combinations of the foregoing from time to time under this prospectus, together with any applicable prospectus supplement, at prices and on terms to be determined by market conditions at the time of offering. This prospectus provides you with a general description of the securities we may offer. At the time we offer a type or series of securities, we will provide a prospectus supplement describing the specific amounts, prices and other important terms of the securities, including, to the extent applicable:

- designation or classification;
- aggregate principal amount or aggregate offering price;
- voting or other rights;
- rates and times of payment of interest, dividends or other payments;
- original issue discount;
- maturity;
- ranking;
- restrictive covenants;
- redemption, conversion, exercise, exchange, settlement or sinking fund terms, including prices or rates, and any provisions for changes to or adjustments in such prices or rates and in the securities or other property receivable upon conversion, exercise, exchange or settlement;
- any securities exchange or market listing arrangements; and
- important U.S. federal income tax considerations.

This prospectus may not be used to offer or sell securities unless accompanied by a prospectus supplement. The prospectus supplement may add, update or change information contained in this prospectus or in documents incorporated by reference in this prospectus. We urge you to read the prospectus supplement related to any securities being offered.

We may sell the securities directly to or through underwriters, dealers or agents. We and our underwriters, dealers or agents reserve the right to accept or reject all or part of any proposed purchase of securities. If we do offer securities through underwriters or agents, we will include in the applicable prospectus supplement (i) the names of the underwriters or agents and applicable fees, discounts and commissions to be paid to them; (ii) details regarding over-allotment options, if any; and (iii) net proceeds to us.

The following descriptions are not complete and may not contain all the information you should consider before investing in any securities we may offer hereunder; they are summarized from, and qualified by reference to, Progenics amended and restated certificate of incorporation, bylaws and the other documents referred to in the descriptions, all of which are or will be publicly filed with the SEC, as applicable. See Where You Can Find More Information.

Capital Stock

Our authorized capital stock consists of 160 million shares of common stock, par value $0.0013 per share, and 20 million shares of preferred stock, par value $0.001 per share. As of November 6, 2013, there were 60,825,404 shares of common stock outstanding, 200,000 held in treasury and 8,992,718 reserved for issuance upon exercise of stock options granted under Company incentive plans. No shares of preferred stock are issued and outstanding.

Table of Contents

Common Stock. Holders of our common stock are entitled to one vote for each share held of record on all matters submitted to a vote of the stockholders. As described in our proxy statement for each Annual Meeting of Stockholders, our By-Laws require that in order to be elected in uncontested elections, a director nominee must receive a majority of the votes cast with respect to such nominee (the number of shares voted for a director nominee must exceed the number of votes cast against that nominee); directors are elected by a plurality vote (*i.e.*, candidates receiving the most votes are elected regardless of whether they constitute a majority) in contested elections. Holders of common stock are not entitled to cumulative voting rights with respect to the election of directors, and as a consequence, minority stockholders are not able to elect directors on the basis of their votes alone. Subject to preferences that may be applicable to any shares of preferred stock currently outstanding or issued in the future which could adversely affect common stockholders as described below, holders of common stock are entitled to receive ratably such dividends as may be declared by our board of directors out of funds legally available therefor. In the event of liquidation, dissolution or winding up of the Company, holders of common stock are entitled to share ratably in all assets remaining after payment of liabilities and the liquidation preference of any then-outstanding preferred stock. Holders of common stock have no preemptive rights and no right to convert their common stock into any other securities. There are no redemption or sinking fund provisions applicable to the common stock. All outstanding shares of common stock are fully paid and non-assessable. American Stock Transfer and Trust Company is the transfer agent and registrar for our common stock.

Preferred Stock. Our board of directors has the authority, without further vote or action by the stockholders, to designate and issue shares of preferred stock in one or more series and to designate the rights, preferences and privileges of each series, which may be greater than the rights of the common stock. We will fix in a certificate of designation the number of shares, the designation and the rights, preferences and privileges, including any dividend, conversion, voting or preemptive rights, terms of redemption, liquidation preferences and sinking fund terms, auction and remarketing procedures, and any transfer or other restrictions or limitations of or relating to any series of preferred stock that we sell under this prospectus and applicable prospectus supplements. The Delaware General Corporation Law (DGCL) provides that in addition to any voting rights that may be provided in the applicable certificate of designation, preferred stock holders have the right to vote separately as a class on a proposed amendment to our charter involving certain fundamental changes in their rights. Preferred stock terms could adversely affect the voting power or other rights of common stock holders and the likelihood that they would receive dividend or liquidation payments, and could have the effect of delaying, deferring or preventing a change in control. You should read the prospectus supplement and the certificate of designation relating to any series of preferred stock we may offer.

Anti-Takeover Effects of Provisions of Delaware Law and Our Charter Documents

Delaware Law

We are subject to the provisions of Section 203 of the DGCL, which, subject to certain exceptions, prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the interested stockholder attained such status with the approval of the board of directors or the business combination is approved in a prescribed manner. A business combination includes a merger or asset sale involving or other transaction resulting in a financial benefit to the interested stockholder. Subject to various exceptions, an interested stockholder is a person who, together with affiliates and associates, owns, or within the past three years did own, 15% or more of a corporation s voting stock. This statute could prohibit or delay the accomplishment of mergers or other takeover or change in control attempts and, accordingly, may discourage attempts to acquire the Company.

Charter Documents

Our bylaws provide that we will indemnify our directors and executive officers to the fullest extent permitted by Delaware law and that we may indemnify our other officers, employees and other agents. We may

Table of Contents

enter into indemnification contracts with our directors and officers and purchase insurance on behalf of any person whom we are required or permitted to indemnify. In addition, our charter provides that the liability of our directors for monetary damages shall be eliminated, except for (i) breach of the directors duty of loyalty to the Company or its stockholders, (ii) acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (iii) violating Section 174 of the DGCL, or (iv) any transaction from which the director derived an improper personal benefit. Pursuant to Delaware law and subject to the foregoing exceptions, our directors shall not be liable for monetary damages for breach of the directors fiduciary duty of care to the Company and its stockholders. This provision does not eliminate the duty of care: in appropriate circumstances, equitable remedies such as injunctive or other forms of non-monetary relief remain available under Delaware law, and it does not affect a director s responsibilities under any other law, such as U.S. federal securities laws or state or federal environmental or other laws.

Debt Securities

We may issue debt securities from time to time, in one or more series, as senior, subordinated or junior subordinated, convertible or non-convertible and secured or unsecured debt. Any senior debt securities will rank equally with any unsubordinated debt. Subordinated debt securities will rank equally with any other subordinated debt of the same ranking we may issue. Convertible debt securities will be convertible into or exchangeable for our common stock or other securities at predetermined conversion rates, and conversion may be mandatory or at the holder s option.

Debt securities will be issued under one or more indentures contracts between us and a national banking association or other eligible party acting as trustee. Following is a summary of certain general features of debt securities we may issue; we will describe the particular terms of any debt securities that we may offer in more detail in the applicable prospectus supplement, which may differ from the terms we describe below. You should read the prospectus supplements, any free writing prospectus we may authorize and the indentures, supplemental indentures and forms of debt securities relating to any series of debt securities we may offer.

General. Except as we may otherwise provide in a prospectus supplement, the relevant indenture will provide that debt securities may be issued from time to time in one or more series. The indenture will not limit the amount of debt securities that may be issued thereunder, and will provide that the specific terms of any series of debt securities shall be set forth in, or determined pursuant to, an authorizing resolution, an officers certificate and/or a supplemental indenture, if any, relating to such series.

We will describe in each prospectus supplement the following terms relating to any series of debt securities:

- the title or designation;
- whether they will be secured or unsecured, and the terms of any security;
- whether the debt securities will be subject to subordination, and any terms thereof;
- any limit upon the aggregate principal amount;
- the date or dates on which the debt securities may be issued and on which we will pay the principal;
- the interest rate, which may be fixed or variable, or the method for determining the rate, the date interest will begin to accrue, the date or dates interest will be payable and the record dates for interest payment dates or the method for determining them;
- the manner in which the amounts of payment of principal of, premium or interest on the debt securities will be determined, if these amounts may be determined by reference to an index based on a currency or currencies other than that in which the debt securities

are denominated or designated to be payable or by reference to a commodity, commodity index, stock exchange index or financial index;

the currency of denomination;

Table of Contents

if payments of principal of, premium or interest will be made in one or more currencies or currency units other than that or those in which the debt securities are denominated, the manner in which the exchange rate with respect to these payments will be determined;

the place or places where the principal of, premium, and interest will be payable, where debt securities of any series may be presented for registration of transfer, exchange or conversion, and where notices and demands to or upon the Company in respect of the debt securities may be made;

the form of consideration in which principal of, premium or interest will be paid;

the terms and conditions upon which we may redeem the debt securities;

any obligation we have to redeem or purchase the debt securities pursuant to any sinking fund, amortization or analogous provisions or at the option of a holder;

the dates on which and the price or prices at which we will repurchase the debt securities at the option of holders and other detailed terms and provisions of these obligations;

the denominations in which the debt securities will be issued, if other than denominations of $1,000 and any integral multiple thereof;

the portion of principal amount payable upon declaration of acceleration of the maturity date, if other than the principal amount;

whether the debt securities are to be issued at any original issuance discount and the amount of discount with which they may be issued;

whether the debt securities will be issued in certificated or global form and, in such case, the depositary and the terms and conditions, if any, upon which interests in such global security or securities may be exchanged in whole or in part for the individual securities represented thereby;

provisions, if any, for defeasance in whole or in part and any addition or change to provisions related to satisfaction and discharge;

the form of the debt securities;

the terms and conditions upon which convertible debt securities will be convertible or exchangeable into securities or property of the Company or another person, if at all, and any additions or changes, if any, to permit or facilitate the same;

provisions, if any, granting special rights to holders upon the occurrence of specified events;

any restriction or condition on transferability;

any addition or change in the provisions related to compensation and reimbursement of the trustee;

any addition to or change in the events of default described in this prospectus or in the indenture and any change in the acceleration provisions so described;

any addition to or change in the covenants described in this prospectus or in the indenture, including terms of any restrictive covenants; and

any other terms which may modify or delete any provision of the indenture.

We may issue debt securities that provide for an amount less than their stated principal amount to be due and payable upon declaration of acceleration of their maturity pursuant to the terms of the indenture. We will provide you with information on the U.S. federal income tax considerations and other special considerations applicable to any debt securities in the applicable prospectus supplement.

Conversion or Exchange Rights. We will set forth in the prospectus supplement the terms, if any, on which a series of debt securities may be convertible into or exchangeable for our common stock or other

Table of Contents

securities. We will include provisions as to whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of shares of our common stock or other securities that the holders of debt securities receive would be subject to adjustment.

Consolidation, Merger or Sale; No Protection in Event of a Change of Control or Highly Leveraged Transaction. Except as we may otherwise provide in a prospectus supplement, the indenture will provide that we may not merge or consolidate with or into another entity, or sell other than for cash or lease all or substantially all our assets to another entity, or purchase all or substantially all the assets of another entity unless we are the surviving entity or, if we are not the surviving entity, the successor, transferee or lessee entity expressly assumes all of our obligations under the indenture or the debt securities, as appropriate.

Unless we state otherwise in the applicable prospectus supplement, the debt securities will not contain any provisions that may afford holders additional protection in the event we have a change of control or in the event of a highly leveraged transaction (whether or not such transaction results in a change of control), which could adversely affect them.

Events of Default Under the Indenture. Except as we may otherwise provide in a prospectus supplement, the following will be events of default under the indenture with respect to any series of debt securities that we may issue:

- if we fail to pay interest when due and our failure continues for 90 days and the time for payment has not been extended or deferred;
- if we fail to pay the principal, or premium, if any, when due whether by maturity or called for redemption;
- if we fail to pay a sinking fund installment, if any, when due and our failure continues for 30 days;
- if we fail to observe or perform any other covenant relating to the debt securities, other than a covenant specifically relating to and for the benefit of holders of another series of debt securities, and our failure continues for 90 days after we receive written notice from the debenture trustee or holders of not less than a majority in aggregate principal amount of the outstanding series; and
- if specified events of bankruptcy, insolvency or reorganization occur as to the Company.

No event of default with respect to a particular series of debt securities (except as to certain events of bankruptcy, insolvency or reorganization) will necessarily constitute an event of default with respect to any other series. The occurrence of an event of default may constitute an event of default under any bank credit agreements we may have in existence from time to time. In addition, the occurrence of certain events of default or an acceleration under the indenture may constitute an event of default under certain of our other indebtedness outstanding from time to time.

Except as we may otherwise provide in a prospectus supplement, if an event of default with respect to debt securities of any series at the time outstanding occurs and is continuing, then the trustee or the holders of not less than a majority in principal amount of the outstanding series may, by a notice in writing to us (and to the debenture trustee if given by the holders), declare to be due and payable immediately the principal (or, if the debt securities are discount securities, that portion of the principal amount as may be specified in the terms of such securities) of and premium and accrued and unpaid interest, if any, on all such debt securities. Before a judgment or decree for payment of the money due has been obtained with respect to any series, the holders of a majority in principal amount of that series (or, at a meeting of holders at which a quorum is present, the holders of a majority in principal amount represented at such meeting) may rescind and annul the acceleration if all events of default, other than the non-payment of accelerated principal, premium, if any, and interest, if any, have been cured or waived as provided in the applicable indenture (including payments or deposits in respect of principal, premium or interest that had become due other than as a result of such acceleration) and the Company has deposited with the indenture trustee or paying agent a sum sufficient to pay all amounts owed to the indenture trustee under the

Table of Contents

indenture, all arrears of interest, if any, and the principal and premium, if any, on the debt securities that have become due other than by such acceleration. We refer you to the relevant prospectus supplement relating to any discount securities for the particular provisions relating to acceleration of a portion of the principal amount thereof upon the occurrence of an event of default.

Subject to the terms of the indenture, and except as we may otherwise provide in a prospectus supplement, if an event of default under the indenture shall occur and be continuing, the debenture trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series, unless such holders have offered the debenture trustee reasonable indemnity. The holders of a majority in principal amount of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the debenture trustee, or exercising any trust or power conferred on the debenture trustee, with respect to that series, provided that, subject to the terms of the indenture, the debenture trustee need not take any action that it believes, upon the advice of counsel, might involve it in personal liability or might be unduly prejudicial to holders not involved in the proceeding.

Except as we may otherwise provide in a prospectus supplement, a holder of the debt securities of any series will only have the right to institute a proceeding under the indenture or to appoint a receiver or trustee, or to seek other remedies if:

- the holder previously has given written notice to the debenture trustee of a continuing event of default with respect to that series;
- the holders of at least a majority in aggregate principal amount outstanding of that series have made written request, and such holders have offered reasonable indemnity to the debenture trustee to institute the proceeding as trustee; and
- the debenture trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount outstanding of that series (or at a meeting of holders at which a quorum is present, the holders of a majority in principal amount of such series represented at such meeting) other conflicting directions within 60 days after the notice, request and offer.

Except as we may otherwise provide in a prospectus supplement, these limitations will not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on, them.

We will periodically file statements with the applicable debenture trustee regarding our compliance with specified covenants in the applicable indenture.

Modification of Indenture; Waiver. Except as we may otherwise provide in a prospectus supplement, the debenture trustee and the Company may, without the consent of any holders, execute a supplemental indenture to change the applicable indenture with respect to specific matters, including, among other things:

- to surrender any right or power conferred upon the Company;
- to provide, change or eliminate any restrictions on payment of principal of or premium, if any; provided that any such action shall not adversely affect the interests of the holders of debt securities of any series in any material respect;
- to change or eliminate any of the provisions of the indenture; provided that any such change or elimination shall become effective only when there is no outstanding debt security created prior to the execution of such supplemental indenture that is entitled to the benefit of such provision and as to which such supplemental indenture would apply;
- to evidence the succession of another entity to the Company;

16

Table of Contents

to evidence and provide for the acceptance of appointment by a successor trustee with respect to one or more series of debt securities and to add or change provisions of the indenture to facilitate the administration of the trusts thereunder by more than one trustee;

to cure any ambiguity, mistake, manifest error, omission, defect or inconsistency in the indenture or to conform the text of any provision in the indenture or in any supplemental indenture to any description thereof in the applicable section of a prospectus, prospectus supplement or other offering document that was intended to be a verbatim recitation of a provision of the indenture or of any supplemental indenture;

to add to or change or eliminate any provision of the indenture as shall be necessary or desirable in accordance with any amendments to the U.S. Trust Indenture Act of 1939;

to make any change in any series of debt securities that does not adversely affect in any material respect the interests of the holders thereof; and

to supplement any of the provisions of the indenture to such extent as shall be necessary to permit or facilitate the defeasance and discharge of any series of debt securities; provided that any such action shall not adversely affect the interests of holders of any debt securities.

In addition, and except as we may otherwise provide in a prospectus supplement, under the indenture the rights of holders of a series of debt securities may be changed by us and the debenture trustee with the written consent of the holders of at least a majority in aggregate principal amount outstanding (or, at a meeting of holders of such series at which a quorum is present, the holders of a majority in principal amount represented at such meeting) that is affected. The debenture trustee and the Company may, however, make the following changes only with the consent of each holder of any outstanding debt securities affected:

extending the fixed maturity;

reducing the principal amount, reducing the rate of or extending the time of payment of interest, or any premium payable upon redemption;

reducing the principal amount of discount securities payable upon acceleration of maturity;

making the principal of or premium or interest payable in currency other than that stated;

impairing the right to institute suit for the enforcement of any payment on or after the fixed maturity date;

materially adversely affecting the economic terms of any right to convert or exchange; and

reducing the percentage of debt securities, the holders of which are required to consent to any amendment or waiver; or modifying, without the written consent of the trustee, the rights, duties or immunities of the trustee.

Except for certain specified provisions, and except as we may otherwise provide in a prospectus supplement, the holders of at least a majority in principal amount of any series (or, at a meeting of holders of such series at which a quorum is present, the holders of a majority in principal amount represented at such meeting) may, on behalf of the holders of all debt securities of that series, waive our compliance with provisions of

the indenture. The holders of a majority in principal amount of the outstanding debt securities of any series may, on behalf of all such holders, waive any past default under the indenture with respect to that series and its consequences, other than a default in the payment of the principal of, premium or any interest; provided, however, that the holders of a majority in principal amount of the outstanding debt securities of any series may rescind an acceleration and its consequences, including any related payment default that resulted from the acceleration.

Discharge. Except as we may otherwise provide in a prospectus supplement, the indenture will provide that we can elect to be discharged from our obligations with respect to one or more series of debt securities. In order to exercise our rights to be discharged, we must deposit with the trustee money or government obligations sufficient to pay all the principal of, the premium, if any, and interest on, the debt securities of the affected series on the dates payments are due.

Table of Contents

Form, Exchange and Transfer. Except as we may otherwise provide in a prospectus supplement, we will issue debt securities only in fully registered form without coupons and, unless we otherwise specify in the applicable prospectus supplement, in denominations of $1,000 and any integral multiple thereof. Except as we may otherwise provide in a prospectus supplement, the indenture will provide that we may issue debt securities in temporary or permanent global form and as book-entry securities that will be deposited with a depositary named by us and identified in a prospectus supplement with respect to that series.

At the option of the holder, subject to the terms of the indenture and the limitations applicable to global securities described in the applicable prospectus supplement, the holder will be able to exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indenture and the limitations applicable to global securities set forth in the applicable prospectus supplement, holders may present the debt securities for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the debt securities or the indenture, we will make no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

We will name in the applicable prospectus supplement the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

Except as we may otherwise provide in a prospectus supplement, if we elect to redeem the debt securities of any series, we will not be required to:

- issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or

- register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Information Concerning the Debenture Trustee. The debenture trustee, other than during the occurrence and continuance of an event of default under the indenture, will undertake to perform only those duties as are specifically set forth in the indenture. Upon an event of default, the debenture trustee must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs. Subject to this provision, the debenture trustee will be under no obligation to exercise any of the powers given it by the indenture at the request of any holder unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

Payment and Paying Agents. Unless we otherwise indicate in the applicable prospectus supplement, we will make payment of interest on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

Unless we otherwise indicate in the applicable prospectus supplement, we will pay principal of and any premium and interest at the office of the indenture trustee or, at the option of the Company, by check payable to the holder. Unless we otherwise indicate in a prospectus supplement, we will designate the corporate trust office

Table of Contents

of the debenture trustee our sole paying agent for payments. We will name in the applicable prospectus supplement any other paying agents that we initially designate. We will maintain a paying agent in each place of payment.

All money we pay to a paying agent or the debenture trustee for the payment of principal or any premium or interest which remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the security thereafter may look only to us for payment thereof.

Governing Law. The indenture and the debt securities will be governed and construed in accordance with the laws of the State of New York.

No Personal Liability of Directors, Officers, Employees and Stockholders. No incorporator, stockholder, employee, agent, officer, director or subsidiary of ours will have any liability for any obligations of ours or, due to the creation of any indebtedness under the debt securities, the indentures or supplemental indentures. The indentures provide that all such liability is expressly waived and released as a condition of, and as consideration for, the execution of such indentures and the issuance of the debt securities.

Warrants, Other Rights and Units

We may from time to time issue warrants or other rights (together, Rights), in one or more series, for the purchase of common stock, preferred stock or debt securities. We may issue Rights independently or together with such securities (as such, Units), and such Rights may be attached to or separate from them. Rights will be evidenced by a Rights certificate issued under one or more Rights agreements between us and a Rights agent which will act solely as our agent in connection with the Rights and will not have any obligation or relationship of agency or trust for or with any holders or beneficial owners of Rights. The forms of any such certificates and agreements will be filed as exhibits to the registration statement of which this prospectus is a part by amendment thereof or as exhibits to a Current Report on Form 8-K incorporated herein by reference, and the accompanying prospectus supplement and such forms may add, update or change the terms and conditions of the Rights or Units described in this prospectus. You should read the prospectus supplements, Rights agreements and Rights certificates that contain the terms of the Rights in their entirety.

The particular terms of each issue of Rights or Units will be described in the applicable prospectus supplement, including, as applicable:

- the title of the Rights;
- any initial offering price;
- the title, aggregate principal amount or number and terms of the securities purchasable upon exercise of the Rights;
- the principal amount or number of securities purchasable upon exercise of each Right and the price at which that principal amount or number may be purchased upon exercise of each Right;
- the currency or currency units in which any offering price and the exercise price are payable;
- the title and terms of any related securities with which the Rights are issued and the number of the Rights issued with each security;
- any date on and after which the Rights and the related securities will be separately transferable;
- any minimum or maximum number of Rights that may be exercised at any one time;

the date on which the right to exercise the Rights will commence and the date on which the right will expire;

a discussion of U.S. federal income tax, accounting or other considerations applicable to the Rights or Units;

Table of Contents

whether the Rights represented by the Rights certificates will be issued in registered or bearer form and, if registered, where they may be transferred and registered;

any anti-dilution provisions of the Rights;

any redemption or call provisions applicable to the Rights;

any provisions for changes to or adjustments in the exercise price; and

any additional terms of the Rights, including terms, procedures and limitations relating to exchange and exercise of the Rights.

Rights certificates will be exchangeable for new Rights certificates of different denominations and, if in registered form, may be presented for registration of transfer, and Rights may be exercised, at the corporate trust office of the Rights agent or any other office indicated in the related prospectus supplement. Before the exercise of Rights, holders of Rights will not be entitled to payments of any dividends, principal, premium or interest on securities purchasable upon exercise of the Rights, to vote, consent or receive any notice as a holder of and in respect of any such securities or to enforce any covenants in any indenture, or to exercise any other rights whatsoever as a holder of securities purchasable upon exercise of the Rights.

PLAN OF DISTRIBUTION

We may sell securities through underwriters or dealers, through agents, directly to one or more purchasers, in at the market offerings, within the meaning of Rule 415(a)(4) under the Securities Act, as amended (Securities Act), to or through a market maker or into an existing trading market, or an exchange or otherwise, or by a combination of these methods. The accompanying prospectus supplement will describe the terms of any offering of securities, including:

the name or names of any underwriters;

the purchase price of the securities and the proceeds we will receive from the sale;

any over-allotment options pursuant to which underwriters may purchase additional securities from us;

any agency fees or underwriting discounts and other items constituting agents or underwriters compensation;

any initial public offering price; and

any discounts or concessions allowed or reallowed or paid to dealers.

If underwriters are used in the sale, they will acquire the securities for their own account and may resell the securities from time to time in one or more transactions at a fixed public offering price or at varying prices determined at the time of the sale. The obligations of the underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. We may offer the securities to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Subject to certain conditions, the underwriters will be obligated to purchase all the securities offered by the prospectus supplement if any such securities are purchased. The underwriters may change from time to time the public offering price and any discounts or concessions allowed or reallowed or paid to dealers. We may use underwriters with whom we have a material relationship, and will describe any such relationships in the prospectus

supplement naming such underwriter(s).

We may sell securities directly or through agents we designate from time to time. We will name any agent involved in the offering and sale of securities, and we will describe in the prospectus supplement any commissions that must be paid to the agent. Unless the prospectus supplement states otherwise, our agent will act on a best-efforts basis for the period of its appointment.

Table of Contents

We may authorize agents or underwriters to solicit offers by certain purchasers to purchase securities at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. The relevant prospectus supplement will set forth the conditions to these contracts and any commissions we must pay for solicitation of these contracts.

We may provide agents and underwriters with indemnification against civil liabilities related to this offering, including liabilities under the U.S. Securities Act of 1933, or contribution with respect to payments that the agents or underwriters may make with respect to these liabilities. Agents and underwriters may engage in transactions with, or perform services for, us in the ordinary course of business.

All securities we may offer, other than common stock, will be new issues of securities with no established trading market. Any underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. We cannot guarantee the liquidity of the trading markets for any securities.

Rules of the SEC may limit the ability of any underwriters to bid for or purchase securities before the distribution of the securities is completed. Underwriters may, however, engage in the following activities in accordance with the rules:

Stabilizing transactions Underwriters may make bids or purchases for the purpose of pegging, fixing or maintaining the price of the securities, so long as stabilizing bids do not exceed a specified maximum.

Over-allotments and syndicate covering transactions Underwriters may sell more securities than those they have committed to purchase in an underwritten offering. This over-allotment creates a short position for the underwriters which may involve either covered short sales or naked short sales. Covered short sales are short sales made in an amount not greater than the underwriters over-allotment option to purchase additional securities in the offering, and may be closed out either by exercising the underwriter s over-allotment option or by purchasing securities in the open market. In determining how they will close the covered short position, the underwriters will consider, among other things, the price of securities available for purchase in the open market as compared to the over-allotment option price. Naked short sales are short sales in excess of the over-allotment option, which the underwriters must close out by purchasing securities in the open market. A naked short position is more likely to be created if the underwriters are concerned that, in the open market after pricing, there may be downward pressure on the price of the securities that could adversely affect investors who purchase securities in the offering.

Penalty bids If underwriters purchase securities in the open market in a stabilizing transaction or syndicate covering transaction, they may reclaim a selling concession from other underwriters and selling group members who sold those securities as part of the offering.

Similar to other purchase transactions, an underwriter s purchases to cover the syndicate short sales or to stabilize the market price of securities may have the effect of raising or maintaining the market price of securities or preventing or mitigating a decline in the market price. As a result, the price of the securities may be higher than the price that might otherwise exist in the open market. The imposition of a penalty bid might also have an effect on the price of securities if it discourages resales of the securities.

If commenced, the underwriters may discontinue at any time any of the activities described above.

Any underwriters who are qualified market makers on The Nasdaq National Market may engage in passive market making transactions in our common stock on The Nasdaq National Market in accordance with Rule 103 of Regulation M, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the common stock. Passive market makers must be identified as such and must comply with applicable volume and price limitations. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker s bid, however, the passive market maker s bid must then be lowered when certain purchase limits are exceeded.

Table of Contents

In connection with the sale of our securities, underwriters or agents may receive compensation from us or from purchasers of the securities, for whom they may act as agents, in the form of discounts, concessions or commissions. Underwriters may sell securities to or through dealers, and these dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters or commissions from the purchasers for whom they may act as agents. Underwriters, dealers and agents that participate in the distribution of securities may be deemed to be underwriters under the Securities Act, and any discounts or commissions they receive from us and any profit on the resale of securities they realize may be deemed to be underwriting discounts and commissions under the Securities Act.

In compliance with guidelines of the Financial Industry Regulatory Authority, the consideration or discount to be received by any FINRA member or independent broker dealer may not exceed eight percent of the aggregate amount of the securities offered pursuant to this prospectus and any applicable prospectus supplement.

To comply with applicable state securities laws, the securities offered by this prospectus will be sold, if necessary, in such jurisdictions only through registered or licensed brokers or dealers. In addition, securities may not be sold in some states unless they have been registered or qualified for sale in the applicable state or an exemption from the registration or qualification requirement is available and is complied with.

Table of Contents

LEGAL MATTERS

The legality of the securities being offered hereby is being passed upon for the Company by David E. Martin, General Counsel, who is the beneficial owner of shares and options to purchase shares of Progenics common stock. Any underwriters will also be advised on legal matters by their own counsel, who will be identified in an applicable prospectus supplement.

EXPERTS

The consolidated financial statements of Progenics Pharmaceuticals, Inc. in Progenics Pharmaceuticals Annual Report (Form 10-K) for the year ended December 31, 2012, and the effectiveness of Progenics Pharmaceuticals internal control over financial reporting as of December 31, 2012, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon, included therein, and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

The financial statements as of December 31, 2011 and for the two years ended December 31, 2011 incorporated in this Prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2012 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

Table of Contents

7,608,696 Shares

Progenics Pharmaceuticals, Inc.

Common Stock

PROSPECTUS SUPPLEMENT

Sole Book-Running Manager

Jefferies

Co-Managers

Needham & Company

Brean Capital

February 21, 2014