ACCELERON PHARMA INC
Form S-1
January 09, 2014

Use these links to rapidly review the document

Table of Contents

As filed with the Securities and Exchange Commission on January 9, 2014

Registration No. 333-

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM S-1

REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

ACCELERON PHARMA INC.

(Exact name of registrant as specified in its charter)

Delaware	**2836**	**27-0072226**
(State or other jurisdiction of incorporation or organization)	(Primary Standard Industrial Classification Code Number)	(I.R.S. Employer Identification Number)

128 Sidney Street
Cambridge, MA 02139
(617) 649-9200

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

John L. Knopf, Ph.D.
Chief Executive Officer and President
128 Sidney Street
Cambridge, MA 02139
(617) 649-9200

(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

Marc Rubenstein, Esq.
Ropes & Gray LLP
Prudential Tower
800 Boylston Street
Boston, MA 02199
(617) 951-7000

John D. Quisel, Ph.D., Esq.
Vice President,
General Counsel and Secretary
Acceleron Pharma Inc.
128 Sidney Street
Cambridge, MA 02139
(617) 649-9200

Jonathan L. Kravetz, Esq.
Brian P. Keane, Esq.
Mintz, Levin, Cohn, Ferris, Glovsky
and Popeo, P.C.
One Financial Center
Boston, MA 02111
(617) 542-6000

Approximate date of commencement of proposed sale to public:
As soon as practicable after this Registration Statement is declared effective.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box. o

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o

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

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

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	**Proposed Maximum Aggregate Offering Price(1)**	**Amount of Registration Fee**
Common Stock, $0.001 par value per share	$115,000,000	$14,812

(1) Estimated solely for the purpose of calculating the registration fee in accordance with Rule 457(o) of the Securities Act of 1933, as amended.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the Registration Statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.

Table of Contents

The information in this preliminary prospectus is not complete and may be changed. This preliminary prospectus is not an offer to sell these securities and we are not soliciting offers to buy these securities in any jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED JANUARY 9, 2014

PRELIMINARY PROSPECTUS

$100,000,000

Common Stock
$ per share

We are selling shares of our common stock.

We have granted the underwriters an option to purchase up to additional shares of common stock.

Our common stock is listed on the NASDAQ Global Market under the symbol "XLRN". On January 8, 2014, the last sale price our common stock was $41.26 per share.

We are an "emerging growth company" as that term is used in the Jumpstart Our Business Startups Act of 2012 and, as such, have elected to comply with certain reduced public company reporting requirements for this prospectus and future filings.

Investing in our common stock involves risk. See "Risk Factors" beginning on page 11.

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

	Per share	Total
Public Offering Price	$	$
Underwriting Discounts and Commissions(1)	$	$
Proceeds to Acceleron (before expenses)	$	$

(1) We refer you to "Underwriting" beginning on page 154 for additional information regarding underwriting compensation.

The underwriters expect to deliver the shares of common stock to investors on or about January , 2014 through the book-entry facilities of The Depositary Trust Company.

Citigroup **Leerink Partners**

Piper Jaffray

JMP Securities

, 2014

Table of Contents

TABLE OF CONTENTS

We are responsible for the information contained in this prospectus and in any free-writing prospectus we prepare or authorize. We have not authorized anyone to provide you with different information, and we take no responsibility for any other information others may give you. 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 not assume that the information contained in this prospectus is accurate as of any date other than the date on the cover of this prospectus.

Trademarks

We own or have rights to trademarks, service marks and trade names that we use in connection with the operation of our business, including our corporate name, logos and website names. Other trademarks, service marks and trade names appearing in this prospectus are the property of their respective owners. The trademarks that we own include Acceleron Pharma®. Solely for convenience, some of the trademarks, service marks and trade names referred to in this prospectus are listed without the ® and symbols, but we will assert, to the fullest extent under applicable law, our rights to our trademarks, service marks and trade names.

Table of Contents

SUMMARY

This summary highlights information contained in other parts of this prospectus. Because it is only a summary, it does not contain all of the information that you should consider before investing in shares of our common stock and it is qualified in its entirety by, and should be read in conjunction with, the more detailed information appearing elsewhere in this prospectus. You should read the entire prospectus carefully, especially "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations", before deciding to buy shares of our common stock. Unless the context requires otherwise, references in this prospectus to "Acceleron", "we", "us" and "our" refer to Acceleron Pharma Inc.

Overview

We are a clinical stage biopharmaceutical company focused on the discovery, development and commercialization of novel protein therapeutics for cancer and rare diseases. Our research focuses on the biology of the Transforming Growth Factor-Beta (TGF-β) protein superfamily, a large and diverse group of molecules that are key regulators in the growth and repair of tissues throughout the human body. We are leaders in understanding the biology of the TGF-β superfamily and in targeting these pathways to develop important new medicines. By coupling our discovery and development expertise, including our proprietary knowledge of the TGF-β superfamily, with our internal protein engineering and manufacturing capabilities, we have built a highly productive research and development platform that has generated innovative clinical and preclinical protein therapeutic candidates with novel mechanisms of action.

We have three internally discovered protein therapeutic candidates that are currently being studied in numerous ongoing Phase 2 clinical trials, focused on cancer and rare diseases. These differentiated protein therapeutic candidates have the potential to significantly improve clinical outcomes for patients.

The Acceleron Discovery and Development Platform: Novel Approaches to Potent Biology

We focus on discovering and developing protein therapeutics that target a group of approximately 30 secreted proteins, or ligands, that are collectively referred to as the TGF-β superfamily. These ligands bind to subsets of 12 different receptors on the surface of cells, triggering intracellular changes in gene expression that guide cell growth and differentiation. The TGF-β superfamily ligands and their receptors represent a diverse and under-explored set of drug targets with the potential to yield therapeutics that modulate the growth and repair of diseased cells and tissues.

Members of the TGF-β superfamily are now recognized as important regulators of red blood cell formation. We have shown that inhibition of members of the TGF-β superfamily ameliorates anemia in mouse models of β- thalassemia and myelodysplastic syndromes (MDS). These red blood cell disorders are generally unresponsive to currently approved drugs. Based on our findings, we are developing two protein therapeutic candidates, sotatercept and ACE- 536, each of which is currently in Phase 2 clinical trials to treat patients with these diseases.

Members of the TGF-β superfamily also play a significant role in regulating blood vessel formation. We and our academic collaborators have shown that mice with a defect in a particular receptor for members of the TGF-β superfamily are resistant to tumor growth due to reduced blood vessel formation in the tumor. We have used this insight to design our anti-angiogenic agent, dalantercept, which is currently in Phase 2 clinical trials for the treatment of cancer.

Sotatercept and ACE-536: Novel Protein Therapeutic Candidates in Phase 2 Clinical Trials for β-thalassemia and MDS

Together with our collaboration partner, Celgene Corporation, we are developing sotatercept and ACE-536, our lead protein therapeutic candidates, to treat anemia and associated complications in patients with β-thalassemia and MDS. Clinical trials are underway in other diseases as well.

Table of Contents

Sotatercept and ACE-536 have already shown promising biological activity in initial clinical trials. We and Celgene have conducted six clinical trials with sotatercept in over 160 healthy volunteers and cancer patients. We have conducted one clinical trial with ACE-536 in healthy volunteers. In these studies, both sotatercept and ACE-536 caused a dose-dependent increase in the number of red blood cells. Based on these results, we and Celgene have initiated Phase 2 clinical trials with each of these protein therapeutic candidates in β-thalassemia and MDS. We and Celgene plan to initiate Phase 3 clinical trials for one or both of these protein therapeutic candidates in one or both of β-thalassemia and MDS by the end of 2014 or early 2015.

β-thalassemia

β-thalassemia is a hereditary disease arising from defects in genes involved in the production of hemoglobin, the protein responsible for carrying oxygen in red blood cells. During red blood cell formation in the bone marrow, these genetic defects cause most of the cells to die before they mature into fully functional red blood cells. As a consequence, patients with β-thalassemia have anemia, a lower than normal number of red blood cells, and many patients experience a broad array of complications arising from their disease, including an enlarged spleen, skeletal deformities and serious organ damage, such as liver fibrosis and heart failure, resulting from the accumulation of iron. There is no approved drug and no effective drug therapy for the anemia of β-thalassemia. Frequent blood transfusions are used to manage the treatment of anemia in patients with β-thalassemia, but further contribute to the accumulation of iron and associated organ toxicities.

We and Celgene have shown that sotatercept and ACE-536 increase the production of red blood cells by promoting their maturation in the bone marrow. We believe this mechanism of action may be particularly beneficial for patients suffering from diseases, such as β-thalassemia, that are characterized by diminished red blood cell maturation. In a mouse model of β-thalassemia, the mouse version of ACE-536 demonstrated broad disease modifying effects. In this model, the mouse version of ACE-536 increased red blood cell production, reduced spleen size, increased bone density and reduced levels of iron in the kidney and liver.

The Thalassaemia International Federation estimates that there are approximately 300,000 patients worldwide with β-thalassemia, approximately 20,000 of which are in the United States and Europe, who are dependent on frequent blood transfusions. We estimate that there are at least as many β-thalassemia patients who do not receive frequent blood transfusions. Many of these patients have hemoglobin levels that are approximately half that of normal individuals and experience significant complications from the disease.

Myelodysplastic Syndromes (MDS)

MDS are a group of heterogeneous hematologic diseases characterized by abnormal proliferation and differentiation of blood precursor cells, including red blood cell precursors, in the bone marrow. This leads to anemia, which is present in the vast majority of MDS patients at the time of diagnosis. Much like the anemia of β-thalassemia, the anemia of MDS is characterized by an over-abundance of early stage red blood cell precursors, a large proportion of which fails to mature into functional red blood cells during the later phases of the red blood cell formation process. Drugs that stimulate the production of early stage red blood cell precursors, such as recombinant erythropoietin, are often used to treat anemia in MDS patients, yet many do not experience a substantial improvement of their anemia with these drugs. Although not approved by the United States Food and Drug Administration (FDA) for use in patients with MDS, these products generate an estimated $500 to $700 million in annual U.S. sales from use in these patients, according to our market research.

Table of Contents

Additional Opportunities for Sotatercept and ACE-536

Although sotatercept and ACE-536 have similar effects on red blood cells, sotatercept has been shown to increase bone mass and biomarkers of bone growth in humans. Many patients with chronic kidney disease suffer from both anemia and bone loss. Celgene is conducting two Phase 2 clinical trials of sotatercept in patients with chronic kidney disease-mineral and bone disorder. Additionally, we have shown that sotatercept inhibits tumor growth in mouse models of multiple myeloma, a cancer of the bone marrow, and sotatercept is being studied in an investigator-sponsored Phase 2 trial in multiple myeloma patients. Celgene and its collaborators continue to explore sotatercept in additional clinical trials including trials in patients with Diamond-Blackfan anemia and myelofibrosis.

Acceleron and Celgene are exploring the preclinical activity of sotatercept and ACE-536 in other red blood cell disorders including sickle cell disease.

Our Partnership with Celgene

We are developing sotatercept and ACE-536 through our exclusive worldwide collaborations with Celgene. As of January 1, 2013, Celgene became responsible for paying 100% of worldwide development costs for both programs. Additionally, we may receive up to $560.0 million of potential development, regulatory and commercial milestone payments and, if these protein therapeutic candidates are commercialized, we will receive a royalty on net sales in the low-to-mid 20% range. If approved, we also will co-promote sotatercept and ACE-536 in North America, for which our commercialization costs will be entirely funded by Celgene.

Dalantercept: Novel Protein Therapeutic Candidate in Phase 2 Clinical Trials for Cancer

Our third clinical stage protein therapeutic candidate, dalantercept, is designed to inhibit blood vessel formation in tumors through a mechanism that is distinct from, and potentially synergistic with, vascular endothelial growth factor (VEGF) pathway inhibitors, the dominant class of cancer drugs that inhibit blood vessel formation. The VEGF pathway inhibitors collectively generate worldwide sales in excess of $8 billion annually. We are developing dalantercept primarily for use in combination with these successful products to produce better outcomes for cancer patients.

Inhibiting Angiogenesis to Limit Tumor Growth

Angiogenesis is a process by which new blood vessels are formed. Angiogenesis can be simplified to two major stages the proliferative stage followed by the maturation stage. During the proliferative stage, vascular endothelial cells, the cells lining the inside of the blood vessels, increase in number. This proliferative stage is followed by the maturation stage during which the endothelial cells coalesce to form tubes which are then stabilized through the recruitment of perivascular cells that form an outer layer of the blood vessels resulting in fully formed, functional vessels.

Tumors depend on angiogenesis to form new blood vessels that supply nutrients and oxygen to feed the rapidly growing malignant cells. The principal molecule driving the proliferative stage of angiogenesis in tumors is a protein called VEGF. Inhibiting VEGF-driven angiogenesis to control tumor growth has become an important and widely-used approach to cancer treatment. There are several FDA-approved cancer drugs that inhibit the VEGF pathway. Despite the success of these drugs, many patients fail to respond or develop resistance to VEGF pathway inhibitor therapy, resulting in an unmet need for new therapies to inhibit angiogenesis by a different mechanism.

We are using our knowledge of the TGF-β superfamily to develop dalantercept, a novel protein therapeutic candidate targeting the maturation stage of angiogenesis. Recently, the activin receptor-like kinase 1 (ALK1) has been recognized as an important regulator of the maturation stage of angiogenesis. ALK1 is one of the 12 receptors for ligands in the TGF-β superfamily and is found

Table of Contents

primarily on endothelial cells. The importance of the ALK1 pathway in angiogenesis was discovered in part through research into a genetic disease in which patients manifest vascular defects, including a reduced ability to form capillary beds, which are the networks of small blood vessels that connect arteries to veins and are necessary for nutrient and waste exchange in tissues. This research revealed that these patients have only one of two functional copies of the ALK1 gene. The resulting decreased signaling through the ALK1 receptor inhibits blood vessel maturation, leading to the reduced formation of capillary beds.

Opportunities for Dalantercept

We reasoned that leveraging the biology of the ALK1 pathway to inhibit maturation of blood vessels could impair the growth of tumors by limiting the development of capillary beds within the tumor. To test this hypothesis, mice with a predisposition to develop tumors were bred to have only one copy, rather than two copies, of the ALK1 gene that normally occur. In response to the loss of half of the ALK1 genes, tumor growth and size and blood vessel density in the tumor were reduced by half. We have also shown in two mouse cancer models that treatment with dalantercept decreases metastases. This is in contrast to VEGF pathway inhibitors, many of which have been shown to increase metastases in mouse cancer models. These results and additional research in the field have established the ALK1 signaling pathway as a promising target for developing a new class of anti-angiogenesis agents, ALK1 pathway inhibitors. We are developing dalantercept to treat cancer by inhibiting the ligands of the TGF-β superfamily that signal through the ALK1 receptor.

We believe one promising opportunity for dalantercept will be its use in combination with VEGF pathway inhibitors because these agents target distinct sequential steps in tumor angiogenesis. Moreover, we believe that dalantercept sensitizes blood vessels to increase the effects of treatment with VEGF pathway inhibitors. A combination of ALK1 and VEGF pathway inhibitors could have application in a number of different oncology indications where VEGF pathway inhibitors are currently used, such as liver cancer, brain cancer, non-small cell lung cancer, colorectal cancer and renal cell carcinoma.

With respect to our third clinical stage protein therapeutic candidate, dalantercept, we have conducted a single agent Phase 1 clinical trial in patients with advanced solid tumors. Additionally, we have studied the single agent activity of dalantercept in a Phase 2 clinical trial in patients with advanced head and neck cancer. Our ongoing focus is on the use of dalantercept in combination with an approved VEGF pathway inhibitor where we have both a mechanistic rationale and supportive preclinical data demonstrating dalantercept in combination with a VEGF pathway inhibitor provides enhanced anti-tumor effects in mice bearing human renal cell carcinoma xenographs. In an ongoing Phase 2 clinical trial of dalantercept in combination with axitinib, an approved VEGF pathway inhibitor, in patients with advanced renal cell carcinoma we have completed the dose escalation stage. We have now initiated the dose expansion phase of this study and plan to start the randomized controlled part of the study at the end of Q1 or early Q2 2014. We also intend to initiate a Phase 2 clinical trial of dalantercept in combination with the VEGF pathway inhibitor sorafenib in patients with liver cancer in the first half of 2014.

We have not entered into a partnership for dalantercept and retain worldwide rights to this program.

ACE-083: Neuromuscular Disorders

In addition to our clinical stage programs, we are developing a protein therapeutic candidate, ACE-083, for a first-in-human clinical trial that we expect to initiate by the end of 2014. ACE-083 has been designed to promote muscle growth in those muscles in which the drug is injected, with minimal systemic effect. We are focused on the development of ACE-083 for diseases in which increases in the size and function of specific muscles may provide a clinical benefit, including inclusion body myositis, facioscapulohumeral dystrophy (FSHD) and disuse atrophy.

Table of Contents

Our Development Pipeline

The status of our three clinical stage protein therapeutic candidates and our most advanced preclinical candidate is summarized below:

Our Strategy

Our goal is to be a leader in the discovery, development and commercialization of novel protein therapeutics for cancer and rare diseases. Key components of our strategy are:

Advance sotatercept and ACE-536 into Phase 3 trials in collaboration with Celgene. We and Celgene are jointly developing sotatercept and ACE-536. Assuming successful completion of the ongoing Phase 2 clinical trials in β-thalassemia and MDS, we plan to initiate Phase 3 clinical trials with Celgene for one or both protein therapeutic candidates in one or both diseases by the end of 2014 or early 2015.

Explore new indications for sotatercept and ACE-536 with Celgene. We and Celgene are continuing our preclinical research to assess the opportunity for sotatercept and ACE-536 to treat certain red blood cell disorders known as hemoglobinopathies, which include diseases such as thalassemias and sickle cell disease. Based on our encouraging preclinical and clinical data in β-thalassemia and our emerging understanding of the mechanism of action of these protein therapeutic candidates, we believe there is a potential for activity for sotatercept and ACE-536 in sickle cell disease, and we continue to explore development of these protein therapeutic candidates for this disease.

Advance dalantercept into Phase 3-enabling clinical trials. Beyond our ongoing Phase 2 clinical trials, in 2014, we plan to initiate additional clinical trials of dalantercept in combination with either an approved anti-angiogenesis agent or chemotherapy in advanced solid tumors. One of these trials is expected to be in patients with liver cancer and other trials

may be in patients with brain cancer, lung cancer or colon cancer.

Table of Contents

Utilize our discovery and development platform to develop additional protein therapeutic candidates. In addition to sotatercept, ACE-536 and dalantercept, all of which were internally discovered using our research and development platform, we intend to continue to discover and develop other protein therapeutics that target and regulate various pathways in the TGF-β superfamily. We plan to bring an additional protein therapeutic candidate, ACE-083, into the clinic in 2014 targeting diseases involving muscle loss. We are also conducting pre-clinical development of ALK1 pathway inhibitors distinct from dalantercept for the treatment of diseases of the eye including age-related macular degeneration. In addition we are developing new protein therapeutic candidates for the treatment of cancer and diseases involving fibrosis.

Strategically leverage collaborations to advance our protein therapeutic candidates. We have received more than $250.0 million from our collaboration partners, including Celgene. Our two collaborations with Celgene for sotatercept and ACE-536 provide us with significant funding and access to Celgene's considerable scientific, development, regulatory and commercial capabilities. We will continue to strategically evaluate possible collaborations where doing so could enhance the development or commercialization of other protein therapeutic candidates in our pipeline.

Establish commercialization and marketing capabilities in North America and potentially other markets. We have retained co-promotion rights in North America for sotatercept and ACE-536, which will be entirely funded by Celgene. We intend to build hematology, oncology and neuromuscular disorder focused specialty sales forces and marketing capability to commercialize our protein therapeutic candidates that receive regulatory approval.

Risk Factors

An investment in our common stock involves a high degree of risk. Any of the factors set forth under "Risk Factors" may limit our ability to successfully execute our business strategy. You should carefully consider all of the information set forth in this prospectus and, in particular, should evaluate the specific factors set forth under "Risk Factors" in deciding whether to invest in our common stock. Among these important risks are the following:

We have incurred net operating losses since our inception and anticipate that we will continue to incur substantial operating losses for the foreseeable future. We may never achieve or sustain profitability.

We will require substantial additional financing to achieve our goals, and a failure to obtain this necessary capital when needed could force us to delay, limit, reduce or terminate our development or commercialization efforts of our protein therapeutic candidates.

If Celgene does not devote sufficient resources to the development of sotatercept and ACE-536, is unsuccessful in its efforts or chooses to terminate its agreements with us, our business will be materially harmed.

If our protein therapeutic candidates fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities, we may incur additional costs or experience delays in completing, or ultimately be unable to complete the development and commercialization of our protein therapeutic candidates.

Our future commercial success depends upon attaining significant market acceptance of our protein therapeutic candidates, if approved, among physicians, patients and health care payers and, if we fail to do so, our business will be materially harmed.

We expect to rely on third parties in the manufacturing and clinical development of our protein therapeutic candidates. If they fail to meet deadlines or perform in an unsatisfactory manner our business could be harmed.

Table of Contents

If we are unable to obtain or protect intellectual property rights related to our protein therapeutic candidates, we may not be able to prevent competitors with the same or similar protein therapeutics from entering our markets.

Implications of Being an Emerging Growth Company

As a company with less than $1.0 billion in revenue during our most recently completed fiscal year, we qualify as an "emerging growth company" as defined in Section 2(a) of the Securities Act of 1933, as amended, which we refer to as the Securities Act, as modified by the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. As an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable, in general, to public companies that are not emerging growth companies. These provisions include:

Reduced disclosure about our executive compensation arrangements;

No non-binding shareholder advisory votes on executive compensation or golden parachute arrangements;

Exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting; and

Reduced disclosure of financial information in this prospectus, including two years of audited financial information and two years of selected financial information.

We may take advantage of these exemptions for up to five years or such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company if we have more than $1.0 billion in annual revenues as of the end of a fiscal year, if we are deemed to be a large-accelerated filer under the rules of the Securities and Exchange Commission, or if we issue more than $1.0 billion of non-convertible debt over a three-year-period.

The JOBS Act permits an emerging growth company to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies. We are choosing to "opt out" of this provision.

Corporate Information

We were incorporated in the state of Delaware in June 2003 as Phoenix Pharma, Inc., and we subsequently changed our name to Acceleron Pharma Inc. and commenced operations in February 2004. Our principal executive offices are located at 128 Sidney Street, Cambridge, Massachusetts 02139, and our telephone number is (617) 649-9200. Our Internet website is *www.acceleronpharma.com*. The information on, or that can be accessed through, our website is not part of this prospectus, and you should not rely on any such information in making the decision whether to purchase our common stock.

Table of Contents

THE OFFERING

Common stock offered by us	shares
Common stock to be outstanding after this offering	shares
Option to purchase additional shares	The underwriters have an option for a period of 30 days to purchase up to additional shares of our common stock.
Use of proceeds	The net proceeds from this offering will be approximately $93.3 million, or approximately $107.4 million if the underwriters exercise their option to purchase additional shares in full, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. We intend to use the net proceeds of this offering (1) to continue development of dalantercept, (2) to conduct clinical trials and associated activities with a new protein therapeutic candidate, ACE-083, (3) to continue to advance and expand our preclinical research pipeline of protein therapeutic candidates and (4) for working capital and other general corporate purposes, including funding the costs of operating as a public company. See "Use of Proceeds".
Risk factors	You should read the "Risk Factors" section of this prospectus for a discussion of factors to consider carefully before deciding to invest in shares of our common stock.
NASDAQ Global Market symbol	XLRN

The number of shares of common stock to be outstanding after this offering is based on 28,348,633 shares of common stock outstanding as of January 1, 2014 and excludes the following:

- 3,942,304 shares of common stock issuable upon exercise of stock options outstanding as of January 1, 2014 at a weighted-average exercise price of $7.05 per share;
- 979,699 shares of common stock issuable upon the exercise of outstanding warrants as of January 1, 2014 at a weighted-average exercise price of $6.53 per share;
- 2,089,945 shares of common stock reserved for future issuance under our 2013 Equity Incentive Plan as of January 1, 2014; and
- 275,000 shares of common stock reserved for future issuance under our Employee Stock Purchase Plan as of January 1, 2014.

Unless otherwise indicated, all information in this prospectus assumes no issuance or exercise of stock options or warrants on or after January 1, 2014 and no exercise of the underwriters' option to purchase up to an additional shares of common stock in this offering.

Table of Contents

SUMMARY FINANCIAL DATA

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

	Year Ended December 31,		Nine Months Ended September 30,	
(in thousands, except per share data)	**2011**	**2012**	**2012**	**2013**
Revenue:				
Collaboration revenue:				
License and milestone	$ 74,406	$ 9,696	$ 7,226	$ 36,044
Cost-sharing, net	4,760	5,558	4,043	9,666
Contract manufacturing	1,745			
Total revenue	80,911	15,254	11,269	45,710
Costs and expenses:				
Research and development	32,713	35,319	25,646	25,834
General and administrative	8,142	8,824	6,318	9,472
Cost of contract manufacturing revenue	1,500			
Total costs and expenses	42,355	44,143	31,964	35,306
Income (loss) from operations	38,556	(28,889)	(20,695)	10,404
Total other expense, net	(2,290)	(3,693)	(1,508)	(14,192)
Net income (loss)	$ 36,266	$ (32,582)	$ (22,203)	$ (3,788)
Comprehensive income (loss)	$ 36,266	$ (32,582)	$ (22,203)	$ (3,788)
Net income (loss) per share applicable to common stockholders(1)				
Basic	$ 0.80	$ (24.84)	$ (17.73)	$ (6.74)
Diluted	$ 0.78	$ (24.84)	$ (17.73)	$ (6.74)
Weighted-average number of common shares used in computing net income (loss) per share applicable to common stockholders				
Basic	2,328	2,401	2,397	3,100
Diluted	2,716	2,401	2,397	3,100

Table of Contents

(in thousands)	September 30, 2013 Actual	As adjusted(2)(3)
Balance Sheet Data:		
Cash and cash equivalents	$ 116,479	$
Total assets	127,260	
Total current liabilities	16,523	
Long-term deferred revenue	6,205	
Long-term notes payable	10,979	
Warrants to purchase common stock	16,526	
Total stockholders' equity	74,564	

(1) See Note 2 within the notes to our financial statements appearing elsewhere in this prospectus for a description of the method used to calculate basic and diluted net income (loss) per common share and pro forma basic and diluted net income (loss) per common share.

(2) As adjusted to reflect the sale of shares of our common stock in this offering at an assumed public offering price of $ per share (the last reported price of our common stock on The NASDAQ Global Market on January , 2014), after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

(3) A $1.00 increase (decrease) in the assumed public offering price of $ per share (the last reported price of our common stock on The NASDAQ Global Market on January , 2014), would increase (decrease) the as adjusted amount of each of cash and cash equivalents and total stockholders' equity by approximately $, assuming that the number of shares offered by us, as set forth on the cover of this prospectus, remains the same and after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

Table of Contents

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below together with all of the other information contained in this prospectus, including our financial statements and the related notes appearing at the end of this prospectus, before deciding to invest in our common stock. If any of the following risks actually occurs, our business, prospects, operating results and financial condition could suffer materially, the trading price of our common stock could decline and you could lose all or part of your investment. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently believe to be immaterial may also adversely affect our business.

Risks related to our financial position and need for additional capital

We have incurred net operating losses since our inception and anticipate that we will continue to incur substantial operating losses for the foreseeable future. We may never achieve or sustain profitability.

We have incurred net losses during most fiscal periods since our inception. As of September 30, 2013, we had an accumulated deficit of $174.2 million. We do not know whether or when we will become profitable. To date, we have not commercialized any products or generated any revenues from the sale of products, and we do not expect to generate any product revenues in the foreseeable future. Our losses have resulted principally from costs incurred in our discovery and development activities.

We anticipate that our expenses will increase in the future as we expand our discovery, research, development, manufacturing and commercialization activities. However, we also anticipate that these increased expenses will be partially offset by milestone payments we expect to receive under our agreements with Celgene and potentially by payments we may receive under new collaboration arrangements we may enter into with third parties for dalantercept or other protein therapeutic candidates. If we do not receive the anticipated milestone payments or do not enter into partnerships for dalantercept or other protein therapeutic candidates on acceptable terms, our operating losses will substantially increase over the next several years as we execute our plan to expand our discovery, research, development, manufacturing and commercialization activities. There can be no assurance that we will enter into a new collaboration or achieve milestones and, therefore, no assurance our losses will not increase prohibitively in the future.

To become and remain profitable, we or our partners must succeed in developing our protein therapeutic candidates, obtaining regulatory approval for them, and manufacturing, marketing and selling those products for which we or our partners may obtain regulatory approval. We or they may not succeed in these activities, and we may never generate revenue from product sales that is significant enough to achieve profitability. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. Our failure to become or remain profitable would depress our market value and could impair our ability to raise capital, expand our business, discover or develop other protein therapeutic candidates or continue our operations. A decline in the value of our company could cause you to lose all or part of your investment.

We will require substantial additional financing to achieve our goals, and a failure to obtain this necessary capital when needed could force us to delay, limit, reduce or terminate our product development or commercialization efforts.

As of September 30, 2013, our cash and cash equivalents were $116.5 million. We believe that we will continue to expend substantial resources for the foreseeable future developing dalantercept and new protein therapeutic candidates. These expenditures will include costs associated with research and development, potentially acquiring new technologies, conducting preclinical studies and clinical trials, potentially obtaining regulatory approvals and manufacturing products, as well as marketing and selling products approved for sale, if any. In addition, other unanticipated costs may arise. Because the

Table of Contents

outcome of our planned and anticipated clinical trials is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of our protein therapeutic candidates.

Celgene pays development, manufacturing and commercialization and certain patent costs for sotatercept and ACE-536. Other than those costs, our future capital requirements depend on many factors, including:

- the scope, progress, results and costs of researching and developing our other protein therapeutic candidates, and conducting preclinical studies and clinical trials;
- the timing of, and the costs involved in, obtaining regulatory approvals for our other protein therapeutic candidates if clinical trials are successful;
- the cost of commercialization activities for our other protein therapeutics, if any of these protein therapeutics is approved for sale, including marketing, sales and distribution costs;
- the cost of manufacturing our other protein therapeutic candidates for clinical trials in preparation for regulatory approval and in preparation for commercialization;
- our ability to establish and maintain strategic partnerships, licensing or other arrangements and the financial terms of such agreements;
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patent claims, including litigation costs and the outcome of such litigation; and
- the timing, receipt, and amount of sales of, or royalties on, our future products, if any.

Based on our current operating plan, we believe that the net proceeds we receive from this offering, together with receipt of anticipated milestone payments and our existing cash and cash equivalents will be sufficient to fund our projected operating requirements into the first quarter of 2017. However, our operating plan may change as a result of many factors currently unknown to us, and we may need additional funds sooner than planned. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. Additional funds may not be available when we need them on terms that are acceptable to us, or at all. If adequate funds are not available to us on a timely basis, we may be required to delay, limit, reduce or terminate preclinical studies, clinical trials or other development activities for one or more of our protein therapeutic candidates or delay, limit, reduce or terminate our establishment of sales and marketing capabilities or other activities that may be necessary to commercialize our protein therapeutic candidates.

Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our technologies or protein therapeutics on unfavorable terms to us.

We may seek additional capital through a variety of means, including through private and public equity offerings and debt financings. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a stockholder. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take certain actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through strategic partnerships with third parties, we may have to relinquish valuable rights to our technologies or protein therapeutics, or grant licenses on terms that are not favorable to us. If we are unable to raise additional funds through equity or debt financing when needed, we may be required to delay, limit, reduce or terminate our product development or commercialization efforts for dalantercept or any protein therapeutics other than sotatercept or

Table of Contents

ACE-536, or grant rights to develop and market protein therapeutics that we would otherwise prefer to develop and market ourselves.

Risks Related to Regulatory Review and Approval of Our Protein Therapeutic Candidates

If we or our partners do not obtain regulatory approval for our current and future protein therapeutics, our business will be adversely affected.

Our protein therapeutic candidates will be subject to extensive governmental regulations relating to, among other things, development, clinical trials, manufacturing and commercialization. In order to obtain regulatory approval for the commercial sale of any protein therapeutic candidates, we or our partners must demonstrate through extensive preclinical studies and clinical trials that the protein therapeutic candidate is safe and effective for use in each target indication. Clinical testing is expensive, time-consuming and uncertain as to outcome. We or our partners may gain regulatory approval for sotatercept, ACE-536, dalantercept, or any other protein therapeutic candidate in some but not all of the territories available or some but not all of the target indications, resulting in limited commercial opportunity for the approved protein therapeutics, or we or they may never obtain regulatory approval for these protein therapeutic candidates.

Delays in the commencement, enrollment or completion of clinical trials of our protein therapeutic candidates could result in increased costs to us as well as a delay or failure in obtaining regulatory approval, or prevent us from commercializing our protein therapeutic candidates on a timely basis, or at all.

We cannot guarantee that clinical trials will be conducted as planned or completed on schedule, if at all. A failure of one or more clinical trials can occur at any stage of testing. Events that may prevent successful or timely commencement, enrollment or completion of clinical development include:

- delays by us or our partners in reaching a consensus with regulatory agencies on trial design;
- delays in reaching agreement on acceptable terms with prospective clinical research organizations, or CROs, and clinical trial sites;
- delays in obtaining required Institutional Review Board, or IRB, approval at each clinical trial site;
- delays in recruiting suitable patients to participate in clinical trials;
- imposition of a clinical hold by regulatory agencies for any reason, including safety concerns or after an inspection of clinical operations or trial sites;
- failure by CROs, other third parties or us or our partners to adhere to clinical trial requirements;
- failure to perform in accordance with the FDA's good clinical practices, or GCP, or applicable regulatory guidelines in other countries;
- delays in the testing, validation, manufacturing and delivery of the protein therapeutic candidates to the clinical sites;
- delays caused by patients not completing participation in a trial or not returning for post-treatment follow-up;
- clinical trial sites or patients dropping out of a trial;

occurrence of serious adverse events in clinical trials that are associated with the protein therapeutic candidates that are viewed to outweigh its potential benefits; or

Table of Contents

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

Delays, including delays caused by the above factors, can be costly and could negatively affect our or Celgene's ability to complete a clinical trial. If we or Celgene are not able to successfully complete clinical trials, we will not be able to obtain regulatory approval and will not be able to commercialize our protein therapeutic candidates.

Clinical failure may occur at any stage of clinical development, and because our protein therapeutic candidates are in an early stage of development, there is a high risk of failure, and we may never succeed in developing marketable products or generating product revenue.

Our early encouraging preclinical and clinical results for sotatercept, ACE-536 and dalantercept are not necessarily predictive of the results of our ongoing or future clinical trials. Promising results in preclinical studies of a drug candidate may not be predictive of similar results in humans during clinical trials, and successful results from early clinical trials of a drug candidate may not be replicated in later and larger clinical trials or in clinical trials for different indications. If the results of our or our partners' ongoing or future clinical trials are inconclusive with respect to the efficacy of our protein therapeutic candidates or if we or they do not meet the clinical endpoints with statistical significance or if there are safety concerns or adverse events associated with our protein therapeutic candidates, we or our partner may be prevented or delayed in obtaining marketing approval for our protein therapeutic candidates. In addition, data obtained from trials and studies are susceptible to varying interpretations, and regulators may not interpret our data as favorably as we do, which may delay or prevent regulatory approval. Alternatively, even if we or our partners obtain regulatory approval, that approval may be for indications or patient populations that are not as broad as intended or desired or may require labeling that includes significant use or distribution restrictions or safety warnings. We or our partners may also be required to perform additional or unanticipated clinical trials to obtain approval or be subject to additional post-marketing testing requirements to maintain regulatory approval. In addition, regulatory authorities may withdraw their approval of a product or impose restrictions on its distribution, such as in the form of a modified risk evaluation and mitigation strategy.

If we or any of our partners violate the guidelines pertaining to promotion and advertising of any of our protein therapeutics, if approved, we or they may be subject to disciplinary action by the FDA's Office of Prescription Drug Promotion (OPDP) or other regulatory authorities.

The FDA's Office of Prescription Drug Promotion, or OPDP, is responsible for reviewing prescription drug advertising and promotional labeling to ensure that the information contained in these materials is not false or misleading. There are specific disclosure requirements, and the applicable regulations mandate that advertisements cannot be false or misleading or omit material facts about the product. Prescription drug promotional materials must present a fair balance between the drug's effectiveness and the risks associated with its use. Most warning letters from OPDP cite inadequate disclosure of risk information.

OPDP prioritizes its actions based on the degree of risk to the public health, and often focuses on newly introduced drugs and those associated with significant health risks. There are two types of letters that OPDP typically sends to companies that violate its drug advertising and promotional guidelines: notice of violation letters, or untitled letters, and warning letters. In the case of an untitled letter, OPDP typically alerts the drug company of the violation and issues a directive to refrain from future violations, but does not typically demand other corrective action. A warning letter is typically issued in cases that are more serious or where the company is a repeat offender. Although we have not received any such letters from OPDP, we or any partner may inadvertently violate OPDP's guidelines in the future and be subject to a OPDP untitled letter or warning letter, which may have a negative impact on our business.

Table of Contents

If we or our partners fail to obtain regulatory approval in jurisdictions outside the United States, we and they will not be able to market our products in those jurisdictions.

We and our partners intend to market our protein therapeutic candidates, if approved, in international markets. Such marketing will require separate regulatory approvals in each market and compliance with numerous and varying regulatory requirements. The approval procedures vary from country-to-country and may require additional testing. Moreover, the time required to obtain approval may differ from that required to obtain FDA approval. In addition, in many countries outside the United States, a protein therapeutic must be approved for reimbursement before it can be approved for sale in that country. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries or by the FDA. The foreign regulatory approval process may include all of the risks associated with obtaining FDA approval. We or our partners may not obtain foreign regulatory approvals on a timely basis, if at all. We or our partners may not be able to file for regulatory approvals and may not receive necessary approvals to commercialize our products in any market.

Even if we or our partners receive regulatory approval for our protein therapeutic candidates, such products will be subject to ongoing regulatory review, which may result in significant additional expense. Additionally, our protein therapeutic candidates, if approved, could be subject to labeling and other restrictions, and we or our partners may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products.

Any regulatory approvals that we or our partners receive for our protein therapeutic candidates may also be subject to limitations on the approved indicated uses for which the product may be marketed or to conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor safety and efficacy. In addition, if the FDA approves any of our protein therapeutic candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for the product will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with current good manufacturing practice, or cGMP, and GCP, for any clinical trials that we or our partners conduct post-approval.

Later discovery of previously unknown problems with an approved protein therapeutic, including adverse events of unanticipated severity or frequency, or with manufacturing operations or processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market, or voluntary or mandatory product recalls;
- fines, warning letters, or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or our partners, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; and
- injunctions or the imposition of civil or criminal penalties.

The FDA's policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our protein therapeutic candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we or our partners are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or not able

Table of Contents

to maintain regulatory compliance, we or our partners may lose any marketing approval that may have been obtained and we may not achieve or sustain profitability, which would adversely affect our business.

Risks Related to Our Reliance on Third Parties

We are dependent on Celgene for the successful development and commercialization of two of our three clinical stage protein therapeutic candidates, sotatercept and ACE-536. If Celgene does not devote sufficient resources to the development of these candidates, is unsuccessful in its efforts, or chooses to terminate its agreements with us, our business will be materially harmed.

We have entered into collaboration agreements with Celgene to develop and commercialize sotatercept and ACE-536. Pursuant to the sotatercept agreement, responsibility for all clinical and other product development activities and for manufacturing sotatercept has been transferred to Celgene. For ACE-536, we are responsible for conducting the two ongoing Phase 2 clinical trials, and we are also responsible for manufacturing supplies for Phase 1 and Phase 2 studies. Celgene will be responsible for all clinical development and manufacturing activities after such studies are completed. As of January 1, 2013, Celgene became responsible for paying 100% of worldwide development costs for sotatercept and ACE-536. We will co-promote sotatercept and ACE-536, if approved by the FDA and its counterparties, in North America. Celgene will be responsible for all commercialization costs, including the cost of our promotion activities.

Celgene is obligated to use commercially reasonable efforts to develop and commercialize sotatercept and ACE-536. Celgene may determine that it is commercially reasonable to develop and commercialize only sotatercept or ACE-536 and discontinue the development or commercialization of the other protein therapeutic candidate, or Celgene may determine that it is not commercially reasonable to continue development of one or both of sotatercept and ACE-536. In the event of any such decision, we may be unable to progress the discontinued candidate or candidates ourselves. In addition, under our collaboration agreements, once Celgene takes over development activities of a protein therapeutic candidate, it may determine the development plan and activities for that protein therapeutic candidate. We may disagree with Celgene about the development strategy it employs, but we will have no rights to impose our development strategy on Celgene. Similarly, Celgene may decide to seek regulatory approval for, and limit commercialization of, either or both of sotatercept and ACE-536 to narrower indications than we would pursue. We would be prevented from developing or commercializing a candidate in an indication that Celgene has chosen not to pursue.

This partnership may not be scientifically or commercially successful due to a number of important factors, including the following:

- Celgene has wide discretion in determining the efforts and resources that it will apply to its partnership with us. The timing and amount of any development milestones, and downstream commercial milestones and royalties that we may receive under such partnership will depend on, among other things, the efforts, allocation of resources and successful development and commercialization of these protein therapeutic candidates by Celgene.

- Celgene may develop and commercialize, either alone or with others, products that are similar to or competitive with the protein therapeutic candidates that are the subject of its partnerships with us. For example, Celgene is currently commercializing and/or developing certain of its existing products, lenalidomide and azacitidine, for certain MDS patients for which sotatercept and ACE-536 are also being developed.

- Celgene may terminate its partnership with us without cause and for circumstances outside of our control, which could make it difficult for us to attract new strategic partners or adversely affect how we are perceived in scientific and financial communities.

Table of Contents

Celgene may develop or commercialize our protein therapeutic candidates in such a way as to elicit litigation that could jeopardize or invalidate our intellectual property rights or expose us to potential liability.

Celgene may not comply with all applicable regulatory requirements, or fail to report safety data in accordance with all applicable regulatory requirements.

If Celgene were to breach its arrangements with us, we may need to enforce our right to terminate the agreement in legal proceedings, which could be costly and cause delay in our ability to receive rights back to the relevant protein therapeutic candidates. If we were to terminate an agreement with Celgene due to Celgene's breach or Celgene terminated the agreement without cause, the development and commercialization of sotatercept and ACE-536 could be delayed, curtailed or terminated because we may not have sufficient financial resources or capabilities to continue development and commercialization of these candidates on our own.

Celgene may enter into one or more transactions with third parties, including a merger, consolidation, reorganization, sale of substantial assets, sale of substantial stock or other change in control, which could divert the attention of its management and adversely affect Celgene's ability to retain and motivate key personnel who are important to the continued development of the programs under the strategic partnership with us. In addition, the third-party to any such transaction could determine to reprioritize Celgene's development programs such that Celgene ceases to diligently pursue the development of our programs and/or cause the respective partnership with us to terminate.

We and Celgene rely on third parties to conduct preclinical studies and clinical trials for our protein therapeutic candidates, and if they do not properly and successfully perform their obligations to us, we may not be able to obtain regulatory approvals for our protein therapeutic candidates.

We design the clinical trials for dalantercept and will do so for any future unpartnered protein therapeutic candidates, and we will continue to work with Celgene on trials for sotatercept and ACE-536. However, we and Celgene rely on CROs and other third parties to assist in managing, monitoring and otherwise carrying out many of these trials. We and Celgene compete with many other companies for the resources of these third parties. The third parties on whom we and Celgene rely generally may terminate their engagements at any time, and having to enter into alternative arrangements would delay development and commercialization of our protein therapeutic candidates.

The FDA and foreign regulatory authorities require compliance with regulations and standards, including GCP, for designing, conducting, monitoring, recording, analyzing, and reporting the results of clinical trials to assure that the data and results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Although we and Celgene rely on third parties to conduct many of our and their clinical trials, we and Celgene are responsible for ensuring that each of these clinical trials is conducted in accordance with its general investigational plan, protocol and other requirements.

If these third parties do not successfully carry out their duties under their agreements, if the quality or accuracy of the data they obtain is compromised due to their failure to adhere to clinical trial protocols or to regulatory requirements, or if they otherwise fail to comply with clinical trial protocols or meet expected deadlines, the clinical trials of our protein therapeutic candidates may not meet regulatory requirements. If clinical trials do not meet regulatory requirements or if these third parties need to be replaced, preclinical development activities or clinical trials may be extended, delayed, suspended or terminated. If any of these events occur, we or Celgene may not be able to obtain regulatory approval of our protein therapeutic candidates on a timely basis or at all.

Table of Contents

We and Celgene intend to rely on third-party manufacturers to make our protein therapeutics, and any failure by a third-party manufacturer may delay or impair our and Celgene's ability to complete clinical trials or commercialize our protein therapeutic candidates.

Manufacturing biologic drugs is complicated and is tightly regulated by the FDA, the European Medicines Agency, or EMA, and comparable regulatory authorities around the world. We currently manufacture drug substance for our preclinical studies, Phase 1 clinical trials and Phase 2 clinical trials of ACE-536 and dalantercept. For Phase 3 and commercial supply of our products that we have not partnered, we expect to use contract manufacturing organizations. Successfully transferring complicated manufacturing techniques to contract manufacturing organizations and scaling up these techniques for commercial quantities will be time consuming and we may not be able to achieve such transfer. Moreover, the market for contract manufacturing services for protein therapeutics is highly cyclical, with periods of relatively abundant capacity alternating with periods in which there is little available capacity. If any need we or Celgene have for contract manufacturing services increases during a period of industry-wide tight capacity, we or Celgene may not be able to access the required capacity on a timely basis or on commercially viable terms.

In addition, we contract with fill & finishing providers with the appropriate expertise, facilities and scale to meet our needs. Failure to maintain cGMP can result in a contractor receiving FDA sanctions, which can impact our and Celgene's contractors' ability to operate or lead to delays in our clinical development programs. We believe that our current fill & finish contractors are operating in accordance with cGMP, but we can give no assurance that FDA or other regulatory agencies will not conclude that a lack of compliance exists. In addition, any delay in contracting for fill & finish services, or failure of the contract manufacturer to perform the services as needed, may delay clinical trials, registration and launches. Any such issues may have a substantial negative effect on our business.

For our two lead products, sotatercept and ACE-536, we rely on our collaboration partner Celgene to produce, or contract for the production of, bulk drug substance and finished drug product for late stage clinical trials and for commercial supplies of any approved candidates. Any failure by Celgene or by third-parties with which Celgene contracts may delay or impair the ability to complete late stage clinical trials or commercialize either or both of sotatercept and ACE-536, if approved.

We produced drug substance for preclinical and Phase 1 and 2 clinical trials for sotatercept and ACE-536. Celgene is now responsible for manufacturing sotatercept and will be responsible for manufacturing ACE-536 for future late-stage clinical trials. Celgene generally does not perform the manufacture of the drug substance or drug product for either sotatercept or ACE-536 itself. Celgene has used and may continue to use contract manufacturers for the manufacture of drug substance and drug product for sotatercept and we have no expectation that Celgene plans to perform the manufacture of bulk drug substance or drug product for either sotatercept or ACE-536 in the future. However, Celgene would have the right to manufacture sotatercept or ACE-536, itself or through the use of contract manufacturers. We understand that they have entered into a manufacturing arrangement for Phase 2 supplies of sotatercept bulk drug substance with contract manufacturers with considerable biotherapeutics manufacturing experience, including manufacturing monoclonal antibodies through processes similar to those used for sotatercept. To date Celgene has not entered into an arrangement with a third party to manufacture supplies of sotatercept or ACE-536 for Phase 3 trials or commercial sales. If they are unable to contract at the appropriate time with a manufacturer willing and able to manufacture sufficient quantities of sotatercept and ACE-536 to meet Phase 3 and commercial demand, either for technical or business reasons, the development and commercialization of sotatercept and ACE-536 may be delayed.

Table of Contents

We may not be successful in establishing and maintaining additional strategic partnerships, which could adversely affect our ability to develop and commercialize products, negatively impacting our operating results.

In addition to our current collaborations with Celgene, a part of our strategy is to strategically evaluate and, as deemed appropriate, enter into additional partnerships in the future when strategically attractive, including potentially with major biotechnology or pharmaceutical companies. We face significant competition in seeking appropriate partners for our protein therapeutic candidates, and the negotiation process is time-consuming and complex. In order for us to successfully partner our protein therapeutic candidates, potential partners must view these protein therapeutic candidates as economically valuable in markets they determine to be attractive in light of the terms that we are seeking and other available products for licensing by other companies. Even if we are successful in our efforts to establish new strategic partnerships, the terms that we agree upon may not be favorable to us, and we may not be able to maintain such strategic partnerships if, for example, development or approval of a protein therapeutic is delayed or sales of an approved product are disappointing. Any delay in entering into new strategic partnership agreements related to our protein therapeutic candidates could delay the development and commercialization of our protein therapeutic candidates and reduce their competitiveness even if they reach the market.

If we fail to establish and maintain additional strategic partnerships related to our protein therapeutic candidates, we will bear all of the risk and costs related to the development of any such protein therapeutic candidate, and we may need to seek additional financing, hire additional employees and otherwise develop expertise for which we have not budgeted. This could negatively affect the development of any unpartnered protein therapeutic candidate.

Risks Related to Our Intellectual Property

If we are unable to obtain or protect intellectual property rights related to our protein therapeutic candidates, we may not be able to compete effectively.

We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our platform technology and protein therapeutic candidates. The patent position of biotechnology companies is generally uncertain because it involves complex legal and factual considerations. The standards applied by the United States Patent and Trademark Office, or USPTO, and foreign patent offices in granting patents are not always applied uniformly or predictably. For example, there is no uniform worldwide policy regarding patentable subject matter or the scope of claims allowable in biotechnology patents. The patent applications that we own or in-license may fail to result in issued patents with claims that cover our protein therapeutic candidates in the United States or in other countries. There is no assurance that all potentially relevant prior art relating to our patents and patent applications has been found. We may be unaware of prior art that could be used to invalidate an issued patent or prevent our pending patent applications from issuing as patents. Even if patents do successfully issue and even if such patents cover our protein therapeutic candidates, third parties may challenge their validity, enforceability or scope, which may result in such patents being narrowed or invalidated. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property, provide exclusivity for our protein therapeutic candidates or prevent others from designing around our claims. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

If patent applications we hold or have in-licensed with respect to our platform or protein therapeutic candidates fail to issue, if their breadth or strength of protection is threatened, or if they fail to provide meaningful exclusivity for our protein therapeutic candidates, it could dissuade companies from collaborating with us. Several patent applications covering our protein therapeutic candidates have been filed recently. We cannot offer any assurances about which, if any, patents will issue, the breadth of any such patents or whether any issued patents will be found invalid and unenforceable or will be threatened

Table of Contents

by third parties. Any successful challenge to these patents or any other patents owned by or licensed to us could deprive us of rights necessary for the successful commercialization of any protein therapeutic candidate that we or our partners may develop. Since patent applications in the United States and most other countries are confidential for a period of time after filing, and some remain so until issued, we cannot be certain that we were the first to file any patent application related to a protein therapeutic candidate. Furthermore, if third parties have filed such patent applications, an interference proceeding in the United States can be initiated by the USPTO or a third party to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. In addition, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after it is filed. Various extensions may be available; however, the life of a patent and the protection it affords is limited. If we encounter delays in obtaining regulatory approvals, the period of time during which we could market a protein therapeutic under patent protection could be reduced. Even if patents covering our protein therapeutic candidates are obtained, once the patent life has expired for a product, we may be open to competition from biosimilar products.

Any loss of patent protection could have a material adverse impact on our business. We and our partner may be unable to prevent competitors from entering the market with a product that is similar to or the same as our protein therapeutics. In addition, the royalty we would receive under our collaboration agreements with Celgene for sotatercept and ACE-536 would be reduced by 50% if such product ceases to be covered by a valid claim of our patents even if no competitor with a similar product has entered the market.

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

Our commercial success depends in part on us and our partners not infringing the patents and proprietary rights of third parties. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions and inter partes reexamination proceedings before the USPTO and corresponding foreign patent offices. Numerous U.S. and foreign issued patents and pending patent applications owned by third parties exist in the fields in which we and our partners are developing and may develop our protein therapeutic candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our protein therapeutic candidates may be subject to claims of infringement of the patent rights of third parties.

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our protein therapeutic candidates, that we failed to identify. For example, applications filed before November 29, 2000 and certain applications filed after that date that will not be filed outside the United States remain confidential until issued as patents. Except for the preceding exceptions, patent applications in the United States and elsewhere are generally published only after a waiting period of approximately 18 months after the earliest filing. Therefore, patent applications covering our platform technology or our protein therapeutic candidates could have been filed by others without our knowledge. Additionally, pending patent applications which have been published can, subject to certain limitations, be later amended in a manner that could cover our platform technologies, our protein therapeutic candidates or the use or manufacture of our protein therapeutic candidates.

If any third-party patents were held by a court of competent jurisdiction to cover aspects of our materials, formulations, methods of manufacture or methods for treatment, the holders of any such patents would be able to block our ability to develop and commercialize the applicable protein therapeutic candidate until such patent expired or unless we or our partners obtain a license. These

Table of Contents

licenses may not be available on acceptable terms, if at all. Even if we or our partners were able to obtain a license, the rights may be nonexclusive, which could result in our competitors gaining access to the same intellectual property. Ultimately, we or our partners could be prevented from commercializing a product, or be forced to cease some aspect of our business operations, if, as a result of actual or threatened patent infringement claims, we or our partners are unable to enter into licenses on acceptable terms. If Celgene is required to enter a license agreement with a third party in order to import, develop, manufacture or commercialize sotatercept or ACE-536, the royalty rate and sales milestone payments that we could receive may be reduced by up to 50%. This could harm our business significantly.

Parties making claims against us or our partners may obtain injunctive or other equitable relief, which could effectively block our or our partners' ability to further develop and commercialize one or more of our protein therapeutic candidates. Defending against claims of patent infringement or misappropriation of trade secrets could be costly and time consuming, regardless of the outcome. Thus, even if we were to ultimately prevail, or to settle at an early stage, such litigation could burden us with substantial unanticipated costs. In addition, litigation or threatened litigation could result in significant demands on the time and attention of our management team, distracting them from the pursuit of other company business. In the event of a successful claim of infringement against us or our partners, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure.

We may face a claim of misappropriation if a third party believes that we inappropriately obtained and used trade secrets of such third party. If we are found to have misappropriated a third party's trade secrets, we may be prevented from further using such trade secrets, limiting our ability to develop our protein therapeutic candidates, and we may be required to pay damages.

During the course of any patent or other intellectual property litigation, there could be public announcements of the results of hearings, rulings on motions, and other interim proceedings in the litigation. If securities analysts or investors regard these announcements as negative, the perceived value of our protein therapeutics, programs, or intellectual property could be diminished. Accordingly, the market price of our common stock may decline.

We have in-licensed a portion of our intellectual property, and, if we fail to comply with our obligations under these arrangements, we could lose such intellectual property rights or owe damages to the licensor of such intellectual property.

We are a party to a number of license agreements that are important to our business, and we may enter into additional license agreements in the future. Our discovery and development platform is built, in part, around patents exclusively in-licensed from academic or research institutions. Certain of our in-licensed intellectual property also covers sotatercept and dalantercept. See "Business Intellectual Property In-Licenses" for a description of our license agreements with the Beth Israel Deaconess Medical Center, the Ludwig Institute for Cancer Research and the Salk Institute for Biological Studies.

Our existing license agreements impose, and we expect that future license agreements will impose, various diligence, milestone payment, royalty and other obligations on us. If there is any conflict, dispute, disagreement or issue of non-performance between us and our licensing partners regarding our rights or obligations under the license agreements, including any such conflict, dispute or disagreement arising from our failure to satisfy payment obligations under any such agreement, we may owe damages, our licensor may have a right to terminate the affected license, and our and our partners' ability to utilize the affected intellectual property in our drug discovery and development efforts, and our ability to enter into collaboration or marketing agreements for an affected protein therapeutic candidate, may be adversely affected.

Table of Contents

For example, the Salk Institute for Biological Studies recently filed a lawsuit against us alleging under one of our license agreements with them, which pertains to ActRIIB, its entitlement to a further share of certain payments received by us under our now-terminated agreement with Shire AG and a share of certain payments received by us under our on-going collaboration agreement with Celgene in connection with ACE-536. Although we and Salk have agreed that ACE-536 is not covered by any patent rights licensed from Salk, an unfavorable outcome in this litigation may lead to us owing significant damages to Salk and higher-than-anticipated future payments under this license in connection with development milestone payments that we may receive from Celgene. It is possible that Salk may seek to terminate the license covering the receptor. We do not believe that such a termination would have a material impact on our business or the development of any of our products. The patents under this license covered only one of our protein therapeutic candidates, ACE-031, the development of which has been discontinued. See "Business Legal Proceedings" for a description of this proceeding.

Confidentiality agreements with employees and third parties may not prevent unauthorized disclosure of trade secrets and other proprietary information.

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable or that we elect not to patent, processes for which patents are difficult to enforce and any other elements of our platform technology and discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. However, trade secrets can be difficult to protect. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, and outside scientific advisors, contractors and collaborators. Although we use reasonable efforts to protect our trade secrets, our employees, consultants, contractors, or outside scientific advisors might intentionally or inadvertently disclose our trade secret information to competitors. In addition, competitors may otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques.

Enforcing a claim that a third party illegally obtained and is using any of our trade secrets is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States sometimes are less willing than U.S. courts to protect trade secrets. Misappropriation or unauthorized disclosure of our trade secrets could impair our competitive position and may have a material adverse effect on our business

Risks Related to Commercialization of Our Protein Therapeutic Candidates

Our future commercial success depends upon attaining significant market acceptance of our protein therapeutic candidates, if approved, among physicians, patients, health care payers and, in cancer markets, acceptance by the operators of major cancer clinics.

Even if we or our partners obtain regulatory approval for sotatercept, ACE-536, dalantercept or any other protein therapeutics that we may develop or acquire in the future, the product may not gain market acceptance among physicians, health care payors, patients and the medical community. Market acceptance of any approved products depends on a number of factors, including:

- the efficacy and safety of the product, as demonstrated in clinical trials;
- the clinical indications for which the product is approved and the label approved by regulatory authorities for use with the product, including any warnings that may be required on the label;
- acceptance by physicians and patients of the product as a safe and effective treatment;
- the cost, safety and efficacy of treatment in relation to alternative treatments;
- the availability of adequate reimbursement and pricing by third party payers and government authorities;
- the continued projected growth of drug markets in our various indications;

Table of Contents

relative convenience and ease of administration;

the prevalence and severity of adverse side effects; and

the effectiveness of our, and our partners' sales and marketing efforts.

Market acceptance is critical to our ability to generate significant revenue. Any protein therapeutic candidate, if approved and commercialized, may be accepted in only limited capacities or not at all. If any approved products are not accepted by the market to the extent that we expect, we may not be able to generate significant revenue and our business would suffer.

Reimbursement may be limited or unavailable in certain market segments for our protein therapeutic candidates, which could make it difficult for us to sell our products profitably.

Market acceptance and sales of any approved protein therapeutics will depend significantly on the availability of adequate coverage and reimbursement from third-party payers and may be affected by existing and future health care reform measures. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which drugs they will pay for and establish reimbursement levels. Reimbursement by a third-party payer may depend upon a number of factors, including the third-party payor's determination that use of a product is:

a covered benefit under its health plan;

safe, effective and medically necessary;

appropriate for the specific patient;

cost-effective; and

neither experimental nor investigational.

Obtaining coverage and reimbursement approval for a product from a government or other third party payer is a time consuming and costly process that could require us to provide supporting scientific, clinical and cost-effectiveness data for the use of our products to the payer. We or our partners may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement. We cannot be sure that coverage or adequate reimbursement will be available for any of our protein therapeutic candidates. Also, we cannot be sure that reimbursement amounts will not reduce the demand for, or the price of, our products. If reimbursement is not available or is available only to limited levels, we may not be able to commercialize certain of our products. In addition in the United States, third-party payers are increasingly attempting to contain health care costs by limiting both coverage and the level of reimbursement of new drugs. As a result, significant uncertainty exists as to whether and how much third-party payers will reimburse patients for their use of newly approved drugs, which in turn will put pressure on the pricing of drugs.

Price controls may be imposed in foreign markets, which may adversely affect our future profitability.

In some countries, particularly member states of the European Union, the pricing of prescription drugs is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after receipt of marketing approval for a product. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. In some countries, we or our partners may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our protein therapeutic candidates

23

Table of Contents

to other available therapies in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third-party payers or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be adversely affected.

The impact of recent healthcare reform legislation and other changes in the healthcare industry and in healthcare spending on us is currently unknown, and may adversely affect our business model.

Our revenue prospects could be affected by changes in healthcare spending and policy in the United States and abroad. We operate in a highly regulated industry and new laws, regulations or judicial decisions, or new interpretations of existing laws, regulations or decisions, related to health care availability, the method of delivery or payment for health care products and services could negatively impact our business, operations and financial condition. There is significant interest in promoting health care reform, as evidenced by the enactment in the United States of the Patient Protection and Affordable Care Act and the Health Care and Education Reconciliation Act in 2010. It is likely that federal and state legislatures within the United States and foreign governments will continue to consider changes to existing health care legislation. We cannot predict the reform initiatives that may be adopted in the future or whether initiatives that have been adopted will be repealed or modified. The continuing efforts of the government, insurance companies, managed care organizations and other payers of healthcare services to contain or reduce costs of healthcare may adversely affect:

- the demand for any drug products for which we may obtain regulatory approval;
- our ability to set a price that we believe is fair for our products;
- our ability to obtain coverage and reimbursement approval for a product;
- our ability to generate revenues and achieve or maintain profitability; and
- the level of taxes that we are required to pay.

We face substantial competition, which may result in others discovering, developing or commercializing products before, or more successfully, than we do.

Our future success depends on our or our partners' ability to demonstrate and maintain a competitive advantage with respect to the design, development and commercialization of our protein therapeutic candidates. Our objective is to design, develop and commercialize new products with superior efficacy, convenience, tolerability and safety. In many cases, the protein therapeutics that we commercialize with our strategic partners or on our own will compete with existing, market-leading products.

There are products currently approved to treat patients with MDS, including iron chelation therapy, immunomodulators and various chemotherapeutic agents. In addition, erythropoiesis stimulating agents and red blood cell transfusions are extensively used to treat anemia in MDS. ACE-536 or sotatercept, if approved, will compete with these therapies. In addition, one or more products not currently approved for the treatment of anemia in MDS may in the future be granted marketing approval for the treatment of anemia in MDS or other conditions for which ACE-536 or sotatercept might be approved, including Aranesp®, being developed by Amgen, which is in Phase 3 trials. While there are currently no drug products approved for the treatment of anemia in β-thalassemia, red blood cell transfusions are extensively used and sotatercept or ACE-536, if approved, would compete with this therapy. In addition, HQK-1001, a fetal hemoglobin stimulating agent being developed by HemaQuest Pharmaceuticals, has completed a Phase 1/2 clinical trial and an investigator sponsored Phase 2 clinical trial in patients with β-thalassemia. Further, the future approval, in one or

Table of Contents

more regions, of a biosimilar product to one of our products could create substantial competition and have a material impact on our business.

Sotatercept or ACE-536, if approved for the treatment of chemotherapy-induced anemia or anemia of chronic kidney disease, would compete with erythropoiesis-stimulating agents, such as Epogen® and Aranesp®, marketed by Amgen, and Procrit®, marketed by Johnson & Johnson, that are currently approved for the treatment of chemotherapy-induced anemia or anemia of chronic kidney disease and other therapies in development including oral, small molecule treatments being developed by Astellas Pharma and Fibrogen designed to increase the body's production of erythropoietin.

While we anticipate that dalantercept, if approved for the treatment of cancer, would likely be approved in combination with certain VEGF pathway inhibitors that are currently approved for the treatment of various cancer types, dalantercept would compete with other products, including other angiogenesis inhibitors, approved for the treatment of these cancers.

Many of our potential competitors have significantly greater financial, manufacturing, marketing, drug development, technical and human resources than we do. Large pharmaceutical companies, in particular, have extensive experience in clinical testing, obtaining regulatory approvals, recruiting patients and in manufacturing pharmaceutical products. These companies also have significantly greater research and marketing capabilities than we do and may also have products that have been approved or are in late stages of development, and have collaborative arrangements in our target markets with leading companies and research institutions. Established pharmaceutical companies may also invest heavily to accelerate discovery and development of novel compounds or to in-license novel compounds that could make the protein therapeutics that we develop obsolete. As a result of all of these factors, our competitors may succeed in obtaining patent protection and/or FDA approval or discovering, developing and commercializing protein therapeutics before we do. In addition, any new product that competes with an approved product must demonstrate compelling advantages in efficacy, convenience, tolerability and safety in order to overcome price competition and to be commercially successful. If we are not able to compete effectively against potential competitors, our business will not grow and our financial condition and operations will suffer.

Our protein therapeutics may cause undesirable side effects or have other properties that delay or prevent their regulatory approval or limit their commercial potential.

Undesirable side effects caused by our protein therapeutics could cause us, Celgene or regulatory authorities to interrupt, delay or halt clinical trials and could result in the denial of regulatory approval by the FDA or other regulatory authorities and potential products liability claims. We and Celgene are currently conducting a number of Phase 2 trials for our clinical stage protein therapeutic candidates. Serious adverse events deemed to be caused by our protein therapeutics could have a material adverse effect on the development of our protein therapeutic candidates and our business as a whole. The most common adverse event to date in the clinical trials evaluating the safety and efficacy of our protein therapeutic candidates has been hypertension in our clinical trials for sotatercept and fluid retention in our clinical trials for dalantercept. Our understanding of the relationship between our protein therapeutic candidates and these events may change as we gather more information, and additional unexpected adverse events may occur. There can be no assurance that additional adverse events associated with our protein therapeutic candidates will not be observed. Recently, we discontinued the development of ACE-031, another of our clinical stage protein therapeutics that binds to ligands of the TGF-β superfamily. Clinical development of ACE-031 was put on clinical hold in 2011 due to preliminary safety observations in patients. After gathering further information from animal toxicology studies, we and our ACE-031 partner, Shire AG, determined that the risk-benefit profile of ACE-031 was not appropriate for the intended patient population, boys aged four and older with a genetic muscle wasting disease, and we discontinued development of this protein therapeutic candidate. As is typical in drug development, we have a program of ongoing toxicology studies in animals for our other clinical stage protein therapeutics and cannot provide assurance that the findings from such studies or any ongoing or future clinical trials will not adversely affect our clinical development activities.

Table of Contents

If we or others identify undesirable side effects caused by our protein therapeutic candidates either before or after receipt of marketing approval, a number of potentially significant negative consequences could result, including:

- our clinical trials may be put on hold;
- we or our partners may be unable to obtain regulatory approval for our protein therapeutic candidates;
- regulatory authorities may withdraw approvals of our protein therapeutic candidates;
- regulatory authorities may require additional warnings on the label;
- a medication guide outlining the risks of such side effects for distribution to patients may be required;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of our protein therapeutics and could substantially increase commercialization costs.

Risks Related to Our Business and Industry

If we fail to attract and keep senior management and key scientific personnel, we may be unable to successfully develop our protein therapeutics, conduct our clinical trials and commercialize our protein therapeutic candidates.

We are highly dependent on members of our senior management, including John L. Knopf, Ph.D., our Chief Executive Officer and President and one of our founders. The loss of the services of any of these persons could impede the achievement of our research, development and commercialization objectives. We do not maintain "key person" insurance for any of our executives or other employees.

Recruiting and retaining qualified scientific, clinical, manufacturing, sales and marketing personnel will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors, including our scientific co-founders, may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us.

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with FDA regulations, to provide accurate information to the FDA, to comply with manufacturing standards we have established, to comply with federal and state healthcare fraud and abuse laws and regulations, to report financial information or data accurately or to disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and

Table of Contents

serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

We may encounter difficulties in managing our growth and expanding our operations successfully.

As we seek to advance our protein therapeutic candidates through clinical trials and commercialization, we will need to expand our development, regulatory, manufacturing, marketing and sales capabilities or contract with third parties to provide these capabilities for us. As our operations expand, we expect that we will need to manage additional relationships with various strategic partners, suppliers and other third parties. Future growth will impose significant added responsibilities on members of management. Our future financial performance and our ability to commercialize our protein therapeutic candidates and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To that end, we must be able to manage our development efforts and clinical trials effectively and hire, train and integrate additional management, administrative and, if necessary, sales and marketing personnel. We may not be able to accomplish these tasks, and our failure to accomplish any of them could prevent us from successfully growing our company.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our protein therapeutics.

We face an inherent risk of product liability as a result of the clinical testing of our protein therapeutic candidates and will face an even greater risk if we commercialize any products. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability, and a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our protein therapeutic candidates. Even a successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

injury to our reputation;

withdrawal of clinical trial participants;

costs to defend the related litigations;

a diversion of management's time and our resources;

substantial monetary awards to trial participants or patients;

product recalls, withdrawals, or labeling, marketing or promotional restrictions;

loss of revenue;

the inability to commercialize our protein therapeutic candidates; and

a decline in our stock price.

Failure to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop. We currently carry product liability insurance covering our clinical trials in the amount of

Table of Contents

$10 million in the aggregate. Although we maintain such insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts.

We must comply with environmental laws and regulations, and failure to comply with these laws and regulations could expose us to significant liabilities.

We use hazardous chemicals and radioactive and biological materials in certain aspects of our business and are subject to a variety of federal, state and local laws and regulations governing the use, generation, manufacture, distribution, storage, handling, treatment and disposal of these materials. Although we believe our safety procedures for handling and disposing of these materials and waste products comply with these laws and regulations, we cannot eliminate the risk of accidental injury or contamination from the use, manufacture, distribution, storage, handling, treatment or disposal of hazardous materials. In the event of contamination or injury, or failure to comply with environmental, occupational health and safety and export control laws and regulations, we could be held liable for any resulting damages and any such liability could exceed our assets and resources. We are uninsured for third-party contamination injury.

Risks Related to Our Common Stock and This Offering

We are eligible to be treated as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, and we cannot be certain if the reduced disclosure requirements applicable to emerging growth companies will make our common stock less attractive to investors.

We are an "emerging growth company", as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including (1) not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, which we refer to as the Sarbanes-Oxley Act, (2) reduced disclosure obligations regarding executive compensation in this prospectus and our periodic reports and proxy statements and (3) exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. In addition, as an emerging growth company, we are only required to provide two years of audited financial statements and two years of selected financial data in this prospectus. We could be an emerging growth company for up to five years, although circumstances could cause us to lose that status earlier, including if the market value of our common stock held by non-affiliates exceeds $700.0 million as of any June 30 before that time or if we have total annual gross revenue of $1.0 billion or more during any fiscal year before that time, in which cases we would no longer be an emerging growth company as of the following December 31 or, if we issue more than $1.0 billion in non-convertible debt during any three-year period before that time, we would cease to be an emerging growth company immediately. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

Under the JOBS Act, emerging growth companies can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

Table of Contents

Our stock price could be highly volatile, and, as a result you may not be able to resell your shares at or above the public offering price.

Since our initial public offering in September 2013, the price of our common stock as reported on The NASDAQ Global Market has ranged from a low of $16.78 on November 6 and 8, 2013 to a high of $43.70 on January 7, 2014. The market price of shares of our common stock could be subject to wide fluctuations in response to many risk factors listed in this section, and others beyond our control, including:

- results of clinical trials of our protein therapeutic candidates, including sotatercept, ACE-536 and dalantercept;
- the timing of the release of results of our clinical trials that are being conducted by Celgene;
- results of clinical trials of our competitors' products;
- regulatory actions with respect to our products or our competitors' products;
- actual or anticipated fluctuations in our financial condition and operating results;
- publication of research reports by securities analysts about us or our competitors or our industry;
- our failure or the failure of our competitors to meet analysts' projections or guidance that we or our competitors may give to the market;
- additions and departures of key personnel;
- strategic decisions by us or our competitors, such as acquisitions, divestitures, spin-offs, joint ventures, strategic investments or changes in business strategy;
- the passage of legislation or other regulatory developments affecting us or our industry;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- sales of our common stock by us, our insiders or our other stockholders;
- speculation in the press or investment community;
- announcement or expectation of additional financing efforts;
- changes in accounting principles;
- terrorist acts, acts of war or periods of widespread civil unrest;

natural disasters and other calamities;

changes in market conditions for biopharmaceutical stocks; and

changes in general market and economic conditions.

In addition, the stock market has recently experienced significant volatility, particularly with respect to pharmaceutical, biotechnology and other life sciences company stocks. The volatility of pharmaceutical, biotechnology and other life sciences company stocks often does not relate to the operating performance of the companies represented by the stock. As we operate in a single industry, we are especially vulnerable to these factors to the extent that they affect our industry or our products, or to a lesser extent our markets. In the past, securities class action litigation has often been initiated against companies following periods of volatility in their stock price. This type of litigation could result in substantial costs and divert our management's attention and resources, and could also require us to make substantial payments to satisfy judgments or to settle litigation.

Table of Contents

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

As of January 1, 2014, our executive officers, directors and principal stockholders, together with their respective affiliates, beneficially owned approximately 43.7% of our common stock, including shares subject to outstanding options and warrants that are exercisable within 60 days after such date, and we expect that upon completion of this offering, that same group will continue to beneficially hold at least % of our outstanding common stock. Accordingly, even after this offering, these stockholders will be able to exert a significant degree of influence over our management and affairs and over matters requiring stockholder approval, including the election of our board of directors and approval of significant corporate transactions. This concentration of ownership could have the effect of entrenching our management and/or the board of directors, delaying or preventing a change in our control or otherwise discouraging a potential acquirer from attempting to obtain control of us, which in turn could have a material and adverse effect on the fair market value of our common stock.

A significant portion of our total outstanding shares may be sold into the public market in the near future, which could cause the market price of our common stock to drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market, or the market perception that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. As of January 1, 2014, based on the number of shares of our common stock then outstanding, assuming (1) the closing of this offering, (2) no exercise of the underwriters' option to purchase additional shares of common stock, and (3) no exercise of outstanding options or warrants, we would have had outstanding an aggregate of approximately shares of common stock. Of these shares, 7,482,723 shares of common stock, including the 6,417,000 shares sold in our initial public offering, and all of the shares of common stock to be sold in this offering, will be freely tradable in the public market without restriction or further registration under the Securities Act of 1933, as amended, or the Securities Act, unless the shares are held by any of our "affiliates" as such term is defined in Rule 144 of the Securities Act. The remaining shares of common stock are "restricted securities" as such term is defined in Rule 144 or are subject to lock up agreements in effect in connection with the initial public offering or entered into in connection with this offering and will be available for sale in the public market are as follows:

Number of Shares and % of Total Outstanding	Date Available for Sale into Public Market
5,896,337 shares, or 21%	March 17, 2014 due to lock up agreements in effect in connection with our initial public offering. However, the representatives of the underwriters can waive the provisions of these lock-up agreements and allow these stockholders to sell their shares at any time.
14,969,573 shares, or 53%	90 days after the date of this prospectus, due to lock-up agreements between the holders of these shares and the underwriters. However, the representatives of the underwriters can waive the provisions of these lock-up agreements and allow these stockholders to sell their shares at any time.

In addition, as of January 1, 2014, there were 979,699 shares subject to outstanding warrants, 3,942,304 shares subject to outstanding options and an additional 2,089,945 shares reserved for future issuance under our employee benefit plans that will become eligible for sale in the public market to the extent permitted by any applicable vesting requirements, the lock-up agreements and Rules 144 and 701 under the Securities Act of 1933, as amended. Moreover, after this offering, holders of an aggregate of approximately 14.8 million shares of our common stock and holders of warrants to purchase 540,097

Table of Contents

shares of our common stock will have rights, subject to some conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. If such holders, by exercising their registration rights, cause a large number of securities to be registered and sold into the public market, these sales could have an adverse effect on the market price for our common stock. These rights have been waived in connection with this offering pursuant to the terms of the registration rights agreement. We have also registered all shares of common stock that we may issue under our 2013 Equity Incentive Plan, and intend to register annual increases pursuant to this plan on a post effective amendment to the registration statement. Once these shares are issued in accordance with the terms of the plans, they can be freely sold in the public market upon issuance, subject to the lock-up agreements and the restrictions imposed on our affiliates under Rule 144. For more information, see "Shares Eligible for Future Sale Rule 144".

You will incur immediate and substantial dilution as a result of this offering.

If you purchase common stock in this offering, you will incur immediate and substantial dilution of $ per share, representing the difference between the assumed public offering price of $ (the last reported price of our common stock on The NASDAQ Global Market on January , 2014) per share and our as adjusted net tangible book value per share after giving effect to this offering. Moreover, in the past we issued warrants and options to acquire common stock at prices significantly below the assumed public offering price. As of January 1, 2014, there were 979,699 shares subject to outstanding warrants and 3,942,304 shares subject to outstanding options. To the extent that these outstanding warrants or options are ultimately exercised, you will incur further dilution.

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

We currently intend to use the net proceeds from this offering to fund the continued development of dalantercept and ACE-083 and to continue to discover and develop other protein therapeutics in our pipeline and for working capital and other general corporate purposes, including funding the costs of operating a public company. See "Use of Proceeds." Any remaining amounts will be used for general corporate purposes, general and administrative expenses, capital expenditures, working capital and prosecution and maintenance of our intellectual property. Although we currently intend to use the net proceeds from this offering in such a manner, we will have broad discretion in the application of the net proceeds. Our failure to apply these funds effectively could affect our ability to continue to develop and commercialize our protein therapeutic candidates.

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

As a newly public company, we are incurring significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act, and rules of the SEC and those of The NASDAQ Global Market, or NASDAQ, have imposed various requirements on public companies including requiring establishment and maintenance of effective disclosure and financial controls. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased and will continue to increase our legal and financial compliance costs and will make some activities more time-consuming and costly.

The Sarbanes-Oxley Act requires, among other things, that we maintain effective internal control over financial reporting and disclosure controls and procedures. In particular, we must perform system and process evaluation and testing of our internal control over financial reporting to allow management to report on the effectiveness of our internal control over financial reporting, as required by Section 404 of the Sarbanes-Oxley Act, beginning with our annual report on Form 10-K for the fiscal

Table of Contents

year ended December 31, 2013. In addition, we will be required to have our independent registered public accounting firm attest to the effectiveness of our internal control over financial reporting beginning with our annual report on Form 10-K following the date on which we are no longer an emerging growth company. Our compliance with Section 404 of the Sarbanes-Oxley Act will require that we incur substantial accounting expense and expend significant management efforts. We currently do not have an internal audit group, and we will need to hire additional accounting and financial staff with appropriate public company experience and technical accounting knowledge. If we are not able to comply with the requirements of Section 404 in a timely manner, or if we or our independent registered public accounting firm identify deficiencies in our internal control over financial reporting that are deemed to be material weaknesses, the market price of our stock could decline and we could be subject to sanctions or investigations by NASDAQ, the SEC or other regulatory authorities, which would require additional financial and management resources.

Our ability to successfully implement our business plan and comply with Section 404 requires us to be able to prepare timely and accurate financial statements. We expect that we will need to continue to improve existing, and implement new operational and financial systems, procedures and controls to manage our business effectively. Any delay in the implementation of, or disruption in the transition to, new or enhanced systems, procedures or controls, may cause our operations to suffer and we may be unable to conclude that our internal control over financial reporting is effective and to obtain an unqualified report on internal controls from our auditors as required under Section 404 of the Sarbanes-Oxley Act. This, in turn, could have an adverse impact on trading prices for our common stock, and could adversely affect our ability to access the capital markets.

We do not expect to pay any cash dividends for the foreseeable future.

You should not rely on an investment in our common stock to provide dividend income. We do not anticipate that we will pay any cash dividends to holders of our common stock in the foreseeable future. Instead, we plan to retain any earnings to maintain and expand our operations. In addition, our ability to pay cash dividends is currently prohibited by the terms of our debt financing arrangement, and any future debt financing arrangement may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. Accordingly, investors must rely on sales of their common stock after price appreciation, which may never occur, as the only way to realize any return on their investment. As a result, investors seeking cash dividends should not purchase our common stock.

Provisions in our restated certificate of incorporation, our amended and restated by-laws and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders, and may prevent attempts by our stockholders to replace or remove our current management.

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

- authorize "blank check" preferred stock, which could be issued by our board of directors without stockholder approval and may contain voting, liquidation, dividend and other rights superior to our common stock;
- create a classified board of directors whose members serve staggered three-year terms;
- specify that special meetings of our stockholders can be called only by our board of directors;
- prohibit stockholder action by written consent;

Table of Contents

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

provide that our directors may be removed only for cause;

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

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

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

require supermajority votes of the holders of our common stock to amend specified provisions of our restated certificate of incorporation and amended and restated by-laws

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

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

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

Our restated certificate of incorporation designates the Court of Chancery of the State of Delaware and federal court within the State of Delaware as the exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our restated certificate of incorporation provides that, subject to limited exceptions, the Court of Chancery of the State of Delaware and federal court within the State of Delaware will be exclusive forums for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, (3) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law, our restated certificate of incorporation or our amended and restated by-laws, or (4) any other action asserting a claim against us that is governed by the internal affairs doctrine. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our restated certificate of incorporation described above. This choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and employees. Alternatively, if a court were to find these provisions of our restated certificate of incorporation inapplicable to, or unenforceable in respect of, one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions, which could adversely affect our business and financial condition.

Table of Contents

Cautionary Note Regarding Forward-Looking Statements

This prospectus contains forward-looking statements. Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based on our current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, our clinical results and other future conditions. The words "anticipate", "believe", "estimate", "expect", "forecast", "goal", "intend", "may", "plan", "predict", "project", "target", "potential", "will", "would", "could", "should", "continue", "contemplate", or the negative of these terms or other similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

The forward-looking statements in this prospectus include, among other things, statements about:

- the timing of results of our ongoing clinical trials;
- our plans to develop and commercialize dalantercept and ACE-083 and our and Celgene's plans to develop and commercialize sotatercept and ACE-536;
- the potential benefits of strategic partnership agreements and our ability to enter into selective strategic partnership arrangements;
- the timing of, and our and Celgene's ability to, obtain and maintain regulatory approvals for our protein therapeutic candidates;
- the rate and degree of market acceptance and clinical utility of any approved protein therapeutic candidate;
- our ability to quickly and efficiently identify and develop protein therapeutic candidates;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our intellectual property position; and
- our estimates regarding expenses, future revenues, capital requirements, the sufficiency of our current and expected cash resources and our need for additional financing.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this prospectus, particularly in the "Risk Factors" section, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

The forward-looking statements in this prospectus represent our views as of the date of this prospectus. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this prospectus.

Table of Contents

USE OF PROCEEDS

The net proceeds of the sale of shares of common stock in this offering will be approximately $93.3 million at the assumed public offering price of $ per share (the last reported price of our common stock on The NASDAQ Global Market on January , 2014), after deducting underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their option to purchase additional shares of common stock in full, we estimate that the net proceeds will be approximately $107.4 million, after deducting underwriting discounts and commissions and estimated offering expenses payable by us. Each $1.00 increase or decrease in the assumed public offering price of $ per share (the last reported price of our common stock on The NASDAQ Global Market on January , 2014) would increase or decrease our net proceeds by approximately $, assuming the number of shares offered by us, as set forth on the cover of this prospectus, remains the same 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 as follows:

- approximately $57.0 million to continue development of dalantercept, including initiation of additional Phase 2 clinical trials of dalantercept in combination with either an approved anti-angiogenesis agent or chemotherapy in advanced solid tumors, and obtaining the supply of dalantercept for Phase 3 clinical studies;

- approximately $8.0 million to conduct clinical trials and associated activities with a new protein therapeutic candidate ACE-083;

- approximately $15.0 million to continue to advance and to expand our preclinical research pipeline of protein therapeutic candidates; and

- use the remainder for general and administrative expenses (including personnel-related costs), potential future development programs, early-stage research and development, capital expenditures and working capital and other general corporate purposes.

The expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. The amounts and timing of our actual expenditures depend on numerous factors, including the ongoing status of and results from our clinical trials and other studies, the progress of our preclinical development efforts and any unforeseen cash needs. As a result, our management will have broad discretion in applying the net proceeds of this offering. Although we may use a portion of the net proceeds of this offering for the acquisition or licensing, as the case may be, of product candidates, technologies, compounds, other assets or complementary businesses, we have no current understandings, agreements or commitments to do so.

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

Table of Contents

MARKET PRICE OF OUR COMMON STOCK

Our common stock has been listed on The NASDAQ Global Market under the symbol "XLRN" since September 19, 2013. Prior to that, there was no public market for our common stock. The following table sets forth for the periods indicated the high and low sales prices per share of our common stock as reported on The NASDAQ Global Market:

Year ended December 31, 2013:	**High**	**Low**
Third quarter(1)	$ 23.41	$ 18.50
Fourth quarter	$ 40.02	$ 16.78
Year ending December 31, 2014:		
First quarter (through January 8, 2014)	$ 43.70	$ 36.86

(1) Represents the period from September 19, 2013, the date on which our common stock first began to trade on The NASDAQ Global Market after the pricing of our initial public offering, through September 30, 2013, the end of our third fiscal quarter.

A recent reported closing price for our common stock is set forth on the cover of this prospectus. Computershare Trust Company, N.A. is the transfer agent and registrar for our common stock. As of January 2, 2014, there were 174 holders of record of our common stock.

Table of Contents

DIVIDEND POLICY

We have never declared or paid cash dividends on our common stock. We currently intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. In addition, our ability to pay cash dividends is currently prohibited by the terms of our debt financing arrangements, and any future debt financing arrangement may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. Any future determination to pay dividends will be made at the discretion of our board of directors.

Table of Contents

CAPITALIZATION

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

- on an actual basis;
- on an as adjusted basis to reflect the sale of shares of our common stock offered in this offering at an assumed public offering price of $ per share (the last reported price of our common stock on The NASDAQ Global Market on January , 2014), after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

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

	As of September 30, 2013	
	Actual	As adjusted(1)
	(in thousands, except share and per share data)	
Cash and cash equivalents	$ 116,479	$
Notes payable, net of current portion	$ 10,979	$
Warrants to purchase common stock	16,526	
Stockholders' equity:		
Undesignated preferred stock, $0.001 par value: 25,000,000 shares authorized and no shares issued or outstanding		
Common stock, $0.001 par value; 175,000,000 shares authorized actual and as adjusted; 28,069,579 shares issued and outstanding, actual, and shares issued and outstanding, as adjusted(2)	35	
Additional paid-in capital	248,750	
Accumulated deficit	(174,221)	
Total stockholders' equity	74,564	
Total capitalization	$ 102,069	$

(1) A $1.00 increase (decrease) in the assumed public offering price of $ per share (the last reported price of our common stock on The NASDAQ Global Market on January , 2014), would increase (decrease) the as adjusted amount of each of cash and cash equivalents and total stockholders' equity by approximately $, assuming that the number of shares offered by us, as set forth on the cover of this prospectus, remains the same and after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

(2) The actual and as adjusted information set forth in the table excludes (i) 3,655,968 shares of common stock issuable upon exercise of stock options outstanding as of September 30, 2013 at a weighted-average exercise price of $4.18 per share, (ii) 1,011,590 shares of common stock issuable upon the exercise of warrants to purchase shares of common stock outstanding as of September 30, 2013 at a weighted-average exercise price of $6.56 per share, (iii) 1,500,000 shares of common stock reserved for future issuance under our 2013 Equity Incentive Plan as of September 30, 2013, and (iv) 275,000 shares of common stock reserved for future issuance under our Employee Stock Purchase Plan as of September 30, 2013.

Table of Contents

SELECTED FINANCIAL DATA

The information set forth below should be read in conjunction with the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section of this prospectus and with our financial statements and notes thereto included elsewhere in this prospectus. The selected financial data in this section are not intended to replace the financial statements and are qualified in their entirety by the financial statements and related notes included elsewhere in this prospectus.

The selected statements of operations and comprehensive income (loss) data for the years ended December 31, 2011 and 2012 and the balance sheet data as of December 31, 2011 and 2012 have been derived from our audited financial statements included elsewhere in this prospectus. The selected statements of operations and comprehensive income (loss) data for the nine months ended September 30, 2012 and 2013 and the balance sheet data as of September 30, 2013 have been derived from our unaudited financial statements included elsewhere in this prospectus. In our opinion, these unaudited financial statements have been prepared on a basis consistent with our audited financial statements and contain all adjustments, consisting only of normal and recurring adjustments, necessary for a fair presentation of such financial data. Our historical results for any prior period are not necessarily indicative of results to be expected in any future period, and our interim period results are not necessarily indicative of results to be expected for a full year or any other interim period.

	Year Ended December 31,		Nine Months Ended September 30,	
(in thousands, except per share data)	**2011**	**2012**	**2012**	**2013**
Revenue:				
Collaboration revenue:				
License and milestone	$ 74,406	$ 9,696	$ 7,226	$ 36,044
Cost-sharing, net	4,760	5,558	4,043	9,666
Contract manufacturing	1,745			
Total revenue	80,911	15,254	11,269	45,710
Costs and expenses:				
Research and development	32,713	35,319	25,646	25,834
General and administrative	8,142	8,824	6,318	9,472
Cost of contract manufacturing revenue	1,500			
Total costs and expenses	42,355	44,143	31,964	35,306
Income (loss) from operations	38,556	(28,889)	(20,695)	10,404
Total other expense, net	(2,290)	(3,693)	(1,508)	(14,192)
Net income (loss)	$ 36,266	$ (32,582)	$ (22,203)	$ (3,788)
Comprehensive income (loss)	$ 36,266	$ (32,582)	$ (22,203)	$ (3,788)
Net income (loss) per share applicable to common stockholders(1)				
Basic	$ 0.80	$ (24.84)	$ (17.73)	$ 6.74
Diluted	$ 0.78	$ (24.84)	$ (17.73)	$ 6.74
Weighted-average number of common shares used in computing net income (loss) per share applicable to common stockholders				
Basic	2,328	2,401	2,397	3,100
Diluted	2,716	2,401	2,397	3,100

Table of Contents

(in thousands)	December 31, 2011	December 31, 2012	September 30, 2013
Balance Sheet Data:			
Cash and cash equivalents	$ 65,037	$ 39,611	$ 116,479
Total assets	73,789	49,212	127,260
Total current liabilities	23,853	38,802	16,523
Long term deferred revenue	33,350	6,760	6,205
Long-term notes payable		16,525	10,979
Warrants to purchase redeemable convertible preferred stock	1,046	1,422	
Warrants to purchase common stock	3,347	5,229	16,526
Redeemable convertible preferred stock	241,549	268,610	
Total stockholder's (deficit) equity	(232,691)	(290,973)	74,564

(1) See Note 2 within the notes to our financial statements appearing elsewhere in this prospectus for a description of the method used to calculate basic and diluted net income (loss) per common share and pro forma basic and diluted net income (loss) per common share.

Table of Contents

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

You should read the following discussion and analysis of financial condition and results of operations together with the section entitled "Selected Financial Data" and our financial statements and related notes included elsewhere in this prospectus. This discussion and other parts of this prospectus contain forward-looking statements that involve risk and uncertainties, such as statements of our plans, objectives, expectations and intentions. Our actual results could differ materially from those discussed in these forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in the "Risk Factors" section.

Overview

We are a clinical stage biopharmaceutical company focused on the discovery, development and commercialization of novel protein therapeutics for cancer and rare diseases. Our research focuses on the biology of the Transforming Growth Factor-Beta (TGF-β) protein superfamily, a large and diverse group of molecules that are key regulators in the growth and repair of tissues throughout the human body. We are leaders in understanding the biology of the TGF-β superfamily and in targeting these pathways to develop important new medicines. By coupling our discovery and development expertise, including our proprietary knowledge of the TGF-β superfamily, with our internal protein engineering and manufacturing capabilities, we have built a highly productive research & development platform that has generated innovative protein therapeutic candidates with novel mechanisms of action. These differentiated protein therapeutic candidates have the potential to significantly improve clinical outcomes for patients with cancer and rare diseases.

We have three internally discovered protein therapeutic candidates that are currently being studied in numerous ongoing Phase 2 clinical trials, focused on cancer and rare diseases. Our two most advanced protein therapeutic candidates, sotatercept and ACE-536, promote red blood cell production through a novel mechanism. Together with our collaboration partner, Celgene Corporation, which we refer to as Celgene, we are developing sotatercept and ACE-536 to treat anemia and associated complications in patients with β-thalassemia and myelodysplastic syndromes (MDS), red blood cell disorders that are generally unresponsive to currently approved drugs. Our third clinical stage protein therapeutic candidate, dalantercept, is designed to inhibit blood vessel formation through a mechanism that is distinct from, and potentially synergistic with, the dominant class of cancer drugs that inhibit blood vessel formation, the vascular endothelial growth factor (VEGF) pathway inhibitors. We are developing dalantercept primarily for use in combination with these successful products to produce better outcomes for cancer patients.

We are developing sotatercept and ACE-536 through our exclusive worldwide collaborations with Celgene. As of January 1, 2013, Celgene became responsible for paying 100% of worldwide development costs for both programs. We may receive up to $560.0 million of potential development, regulatory and commercial milestone payments still outstanding and, if these protein therapeutic candidates are commercialized, we will receive a royalty on net sales in the low-to-mid 20% range. We also will co-promote sotatercept and ACE-536 in North America, if approved, for which our commercialization costs will be entirely funded by Celgene. We have not entered into a partnership for dalantercept and retain worldwide rights to this program.

As of September 30, 2013, our operations have been primarily funded by $105.1 million in equity investments from venture investors, $86.8 million in net proceeds from our initial public offering, $49.2 million in equity investments from our partners and $192.6 million in upfront payments, milestones, and net research and development payments from our strategic partners.

Table of Contents

We expect to continue to incur significant expenses and increasing operating losses over at least the next several years. We expect our expenses will increase substantially in connection with our ongoing activities, as we:

- conduct clinical trials for dalantercept;
- continue our preclinical studies and potential clinical development efforts of our existing preclinical protein therapeutic candidates;
- continue research activities for the discovery of new protein therapeutics;
- manufacture protein therapeutics for our preclinical studies and clinical trials;
- seek regulatory approval for our protein therapeutics; and
- operate as a public company.

We will not generate revenue from product sales unless and until we or a partner successfully complete development and obtain regulatory approval for one or more of our protein therapeutic candidates, which we expect will take a number of years and is subject to significant uncertainty. All current and future development and commercialization costs for sotatercept and ACE-536 are paid by Celgene. If we obtain regulatory approval for dalantercept or any future protein therapeutic candidate, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution to the extent that such costs are not paid by future partners. We will seek to fund our operations through the sale of equity, debt financings or other sources, including potential additional collaborations. However, we may be unable to raise additional funds or enter into such other arrangements when needed on favorable terms, or at all. If we fail to raise capital or enter into such other arrangements as, and when, needed, we may have to significantly delay, scale back or discontinue the development or commercialization of one or more of our protein therapeutics.

Our ability to generate product revenue and become profitable depends upon our and our partners' ability to successfully commercialize products. We expect to incur losses for the foreseeable future, and we expect these losses to increase as we continue our development of, and seek regulatory approvals for, our protein therapeutics and potentially begin to commercialize any approved products. For a description of the numerous risks and uncertainties associated with product development, see "Risk Factors".

Financial Operations Overview

Revenue

Collaboration Revenue

We have not generated any revenue from the sale of products. Our revenue to date has been predominantly derived from collaboration revenue, which includes license and milestone revenues and cost sharing revenue, generated through collaboration and license agreements with partners for the development and commercialization of our protein therapeutics. Cost sharing revenue represents amounts reimbursed by our collaboration partners for expenses incurred by us for research and development activities and, potentially, co-promotion activities, under our collaboration agreements. Cost sharing revenue is recognized in the period that the related activities are performed. To the extent that we reimburse collaborators for costs incurred in connection with activities performed by them, we record these costs as a reduction of cost-sharing revenue.

Table of Contents

Contract Manufacturing Revenue

We have generated contract manufacturing revenue in the past but have no current contract manufacturing arrangements. Contract manufacturing revenue consists of revenue received for producing bulk drug substance for third parties other than our partners.

Costs and Expenses

Research and Development Expenses

Research and development expenses consist primarily of costs directly incurred by us for the development of our protein therapeutic candidates, which include:

- direct employee-related expenses, including salaries, benefits, travel and stock-based compensation expense of our research and development personnel;
- expenses incurred under agreements with clinical research organizations, or CROs, and investigative sites that will conduct our clinical trials;
- the cost of acquiring and manufacturing preclinical and clinical study materials and developing manufacturing processes;
- allocated facilities, depreciation, and other expenses, which include rent and maintenance of facilities, insurance and other supplies;
- expenses associated with obtaining and maintaining patents; and
- costs associated with preclinical activities and regulatory compliance.

Research and development costs are expensed as incurred. Costs for certain development activities are recognized based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors and our clinical sites.

We cannot determine with certainty the duration and completion costs of the current or future clinical trials of our protein therapeutic candidates or if, when, or to what extent we will generate revenues from the commercialization and sale of any of our protein therapeutic candidates for which we or any partner obtain regulatory approval. We or our partners may never succeed in achieving regulatory approval for any of our protein therapeutic candidates. The duration, costs and timing of clinical trials and development of our protein therapeutic candidates will depend on a variety of factors, including:

- the scope, rate of progress, and expense of our ongoing, as well as any additional, clinical trials and other research and development activities;
- future clinical trial results;
- potential changes in government regulation; and
- the timing and receipt of any regulatory approvals.

A change in the outcome of any of these variables with respect to the development of a protein therapeutic candidate could mean a significant change in the costs and timing associated with the development of that protein therapeutic candidate. For example, if the FDA, or another regulatory authority were to require us to conduct clinical trials beyond those that we currently anticipate will be required for the completion of the clinical development of protein therapeutics, or if we experience significant delays in the enrollment in any clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development.

Table of Contents

From inception through September 30, 2013, we have incurred $277.0 million in research and development expenses. We plan to increase our research and development expenses for the foreseeable future as we continue the development of our TGF-β platform protein therapeutics, the discovery and development of preclinical protein therapeutics, including ACE-083, and the development of sotatercept, ACE-536 and dalantercept. Beginning January 1, 2013, expenses associated with sotatercept and ACE-536 are reimbursed 100% by Celgene. These reimbursements are recorded as revenue. Of the Phase 2 clinical trials that are underway for sotatercept, ACE-536 and dalantercept, we are expensing the costs of six clinical trials of ACE-536 and dalantercept, of which the two for ACE-536 are reimbursed by Celgene.

We manage certain activities such as clinical trial operations, manufacture of protein therapeutic candidates, and preclinical animal toxicology studies through third-party CROs. The only costs we track by each protein therapeutic candidate are external costs such as services provided to us by CROs, manufacturing of preclinical and clinical drug substance, and other outsourced research and development expenses. We do not assign or allocate to individual development programs internal costs such as salaries and benefits, facilities costs, lab supplies and the costs of preclinical research and studies. Our external research and development expenses for sotatercept, ACE-536, dalantercept and ACE-031 (for which development was suspended in April 2013) during the years ended December 31, 2011 and 2012 and the nine months ended September 30, 2012 and 2013 are as follows:

	Year Ended December 31,		Nine Months Ended September 30,	
(in thousands)	**2011**	**2012**	**2012**	**2013**
Sotatercept(1)	$ 974	$ 6	$ 6	$ 1
ACE-536(1)	681	2,885	2,047	3,182
Dalantercept	1,323	3,422	2,220	3,413
ACE-031(2)	4,240	3,453	2,442	997
Total direct research and development expenses	7,218	9,766	6,715	7,593
Other expenses(3)	25,495	25,553	18,931	18,241
Total research and development expenses	$ 32,713	$ 35,319	$ 25,646	$ 25,834

(1) Beginning January 1, 2013, expenses associated with sotatercept and ACE-536 are reimbursed 100% by Celgene. These reimbursements are recorded as revenue and are presented as cost-sharing, net.

(2) In April 2013, we and Shire AG, which we refer to as Shire, determined not to further advance the development of ACE-031, and Shire terminated our collaboration agreement, effective as of June 30, 2013.

(3) Other expenses include unallocated employee and contractor-related expenses, facility expenses and miscellaneous expenses.

Contract Manufacturing Expenses

Contract manufacturing expenses consist primarily of costs incurred for the production of bulk drug substance for third parties other than our partners. The costs generally include employee-related expenses including salary and benefits, direct materials and overhead costs including rent, depreciation, utilities, facility maintenance and insurance. We do not have any current contract manufacturing arrangements.

Table of Contents

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and related costs for personnel, including stock-based compensation and travel expenses for our employees in executive, operational, finance and human resource functions and other general and administrative expenses including directors' fees and professional fees for accounting and legal services.

Since the completion of our initial public offering in September 2013, we have experienced increased expenses related to audit, legal, regulatory and tax-related services associated with maintaining compliance with exchange listing and Securities and Exchange Commission requirements, director and officer insurance premiums, and investor relations costs associated with being a public company. We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support our continued research and development and potential commercialization of our protein therapeutics. Additionally, if and when we believe regulatory approval of a protein therapeutic candidate appears likely, to the extent that we are undertaking commercialization of such protein therapeutic candidate ourselves, we anticipate an increase in payroll and related expenses as a result of our preparation for commercial operations.

Other Expense, Net

Other expense, net consists primarily of interest expense from our venture debt facility, interest income earned on cash and cash equivalents, and the re-measurement gain or loss associated with the change in the fair value of our preferred stock and common stock warrant liabilities.

We use the Black-Scholes option pricing model to estimate the fair value of the warrants. We base the estimates in the Black-Scholes option pricing model, in part, on subjective assumptions, including stock price volatility, risk-free interest rate, dividend yield, and the fair value of the preferred stock or common stock underlying the warrants.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations are based on our financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, and expenses and the disclosure of contingent assets and liabilities in our financial statements. On an ongoing basis, we evaluate our estimates and judgments, including those related to revenue recognition, accrued expenses and stock-based compensation. We also utilize significant estimates and assumptions in determining the fair value of our common stock and the fair value of our liability-classified warrants to purchase preferred stock and common stock. We base our estimates on historical experience, known trends and events, and various other factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in the notes to our financial statements appearing elsewhere in this prospectus, we believe the following accounting policies to be most critical to the judgments and estimates used in the preparation of our financial statements.

Revenue Recognition

We have primarily generated revenue through collaboration arrangements with strategic partners for the development and commercialization of our protein therapeutics.

Table of Contents

We recognize revenue in accordance with Accounting Standards Codification (ASC) Topic 605, *Revenue Recognition*. Accordingly, revenue is recognized for each unit of accounting when all of the following criteria are met: (1) persuasive evidence of an arrangement exists; (2) delivery has occurred or services have been rendered; (3) the fee is fixed or determinable; and (4) collectability is reasonably assured.

Amounts received prior to satisfying the revenue recognition criteria are recorded as deferred revenue on our balance sheets. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, current portion and amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, net of current portion.

Under collaboration agreements, we may receive payments for non-refundable up-front fees, milestone payments upon achieving significant development events, research and development reimbursements and royalties on future product sales. These payments are received in connection with the deliverables contained in the arrangements which may include (1) licenses, or options to obtain licenses, to our technology, (2) research and development activities performed for the collaboration partner, (3) participation on joint committees and (4) manufacturing clinical or preclinical material.

Effective January 1, 2011, we adopted Accounting Standards Update (ASU) No. 2009-13, *Multiple-Deliverable Revenue Arrangements*, which amends ASC Topic 605-25, *Revenue Recognition Multiple Element Arrangements*. This guidance applies to new arrangements as well as existing agreements that are significantly modified after January 1, 2011.

The application of the multiple element guidance requires subjective determinations, and requires management to make judgments about the individual deliverables, and whether such deliverables are separable from the other aspects of the contractual relationship. Deliverables are considered separate units of accounting provided that: (1) the delivered item(s) has value to the customer on a stand-alone basis and (2) if the arrangement includes a general right of return relative to the delivered item(s), delivery or performance of the undelivered item(s) is considered probable and substantially in our control. In determining the units of accounting, management evaluates certain criteria, including whether the deliverables have stand-alone value, based on the consideration of the relevant facts and circumstances for each arrangement, such as the research, manufacturing and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. In addition, we consider whether the collaboration partner can use the other deliverable(s) for their intended purpose without the receipt of the remaining element(s), whether the value of the deliverable is dependent on the undelivered item(s), and whether there are other vendors that can provide the undelivered element(s).

Arrangement consideration that is fixed or determinable is allocated among the separate units of accounting using the relative selling price method, and the applicable revenue recognition criteria, as described above, are applied to each of the separate units of accounting in determining the appropriate period or pattern of recognition. We determine the estimated selling price for deliverables within each agreement using vendor-specific objective evidence (VSOE) of selling price, if available, third-party evidence (TPE) of selling price if VSOE is not available, or management's best estimate of selling price (BESP) if neither VSOE nor TPE is available. Subsequent to the adoption of ASU 2009-13, we typically use BESP to estimate the selling price of the deliverables. Determining the BESP for a unit of accounting requires significant judgment. In developing the BESP for a unit of accounting, we consider applicable market conditions and relevant entity-specific factors, including factors that were contemplated in negotiating the agreement with the customer and estimated costs. We validate the BESP for units of accounting by evaluating whether changes in the key assumptions used to determine the BESP will have a significant effect on the allocation of arrangement consideration between multiple units of accounting.

Table of Contents

Our agreements may contain options which provide the collaboration partner the right to obtain additional licenses. Options are considered substantive if, at the inception of the arrangement, we are at risk as to whether the collaboration partner will choose to exercise the option. Factors that we consider in evaluating whether an option is substantive include the overall objective of the arrangement, the benefit the collaborator might obtain from the arrangement without exercising the option, the cost to exercise the option and the likelihood that the option will be exercised. For arrangements under which an option is considered substantive, we do not consider the item underlying the option to be a deliverable at the inception of the arrangement and the associated option fees are not included in allocable arrangement consideration, assuming the option is not priced at a significant and incremental discount. Conversely, for arrangements under which an option is not considered substantive or if an option is priced at a significant and incremental discount, we would consider the item underlying the option to be a deliverable at the inception of the arrangement and a corresponding amount would be included in allocable arrangement consideration.

We typically receive up-front, non-refundable payments when licensing our intellectual property in conjunction with a research and development agreement. When we believe the license to our intellectual property has stand-alone value, we generally recognize revenue attributed to the license upon delivery. When we believe the license to our intellectual property does not have stand-alone value from the other deliverables to be provided in the arrangement, we generally recognize revenue attributed to the license on a straight-line basis over our contractual or estimated performance period, which is typically the term of our research and development or manufacturing obligations. We continually evaluate these periods, and will adjust the period of revenue recognition if circumstances change.

Research and development funding is recognized as revenue in the period that the related services are performed. When we act as the principal under our collaboration arrangements, we record payments received for the reimbursement of research and development costs as cost-sharing revenue. To the extent that we reimburse the collaborator for costs incurred, we record these costs as a reduction of cost-sharing revenue.

We periodically review the basis for our estimates, and we may change the estimates if circumstances change. These changes can significantly increase or decrease the amount of revenue recognized. As we apply our policy to our collaboration arrangements we make judgments which affected the pattern of revenue recognition. For instance, in our arrangement with Celgene, we are obligated to provide research and development services. We are recognizing revenue over the estimated period of our performance of the research and development services, which was estimated to end in December 2014, the expected completion date of the proof-of-concept trials for ACE-536 under the Celgene collaboration. Another instance relates to our arrangement with Shire AG, where in April 2013, we and Shire determined not to further advance the development of ACE-031 or back-up compounds and Shire terminated our collaboration agreement effective as of June 30, 2013.

In addition to up-front payments and research and development funding, we may also be entitled to milestone payments that are contingent upon achievement of a predefined objective. At the inception of each arrangement that includes milestone payments, we evaluate whether the milestone is substantive and at-risk. This evaluation includes an assessment of whether (1) the consideration is commensurate with either the entity's performance to achieve the milestone, or the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting at least in part from the entity's performance to achieve the milestone, (2) the consideration relates solely to past performance, and (3) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. We evaluate factors such as the scientific, regulatory, commercial and other risks that must be overcome to achieve the respective milestone, the level of effort and investment required to achieve the respective milestone, and whether the milestone consideration is reasonable relative to all deliverables and payment terms in the arrangement in making this assessment. On the milestone

Table of Contents

achievement date, assuming all other revenue recognition criteria are met and the milestone is deemed substantive and at-risk, we recognize the payment as license and milestone revenue. For milestones that are not deemed substantive and at-risk, where payment is reasonably assured, we recognize the milestone payment over the remaining service period.

Sales and commercial milestones and royalties will be recognized when and if earned, provided collectability is reasonably assured.

Clinical Trial Accruals and Related Expenses

We accrue and expense costs for clinical trial activities performed by third parties, including CROs and clinical investigators, based upon estimates made as of the reporting date of the work completed over the life of the individual study in accordance with agreements established with CROs and clinical trial sites. Some CROs invoice us on a monthly basis, while others invoice upon achievement of milestones and the expense is recorded as services are rendered. We determine the estimates of clinical activities incurred at the end of each reporting period through discussion with internal personnel and outside service providers as to the progress or stage of completion of trials or services, as of the end of each reporting period, pursuant to contracts with numerous clinical trial centers and CROs and the agreed upon fee to be paid for such services. The significant factors considered in estimating accruals include the number of patients enrolled and the percentage of work completed to date. Costs of setting up clinical trial sites for participation in the trials that are paid for in advance are expensed over the estimated set-up period. While the set-up periods vary from one arrangement to another, such set-up periods generally take approximately three months. Set-up activities include clinical site identification, institutional review board, or IRB, submissions, regulatory submissions, clinical investigator kick-off meetings and pre-study site visits. Clinical trial site costs related to patient enrollments are accrued as patients are entered into the trial.

Stock-Based Compensation

We account for our stock-based awards in accordance with ASC Topic 718, *Compensation Stock Compensation*, or ASC 718, which requires all stock-based payments to employees, including grants of employee stock options and modifications to existing stock options, to be recognized in the statements of operations and comprehensive income (loss) based on their fair values. We recognize the compensation cost of awards subject to service-based vesting conditions over the requisite service period, which is generally equal to the vesting term. For awards subject to both performance and service-based vesting conditions, we recognize compensation cost using an accelerated recognition method when it is probable that the performance condition will be achieved. We account for stock-based awards to non-employees using the fair value method. Stock options granted to non-employees are subject to periodic revaluation over their vesting terms and stock-based compensation cost is recognized using an accelerated recognition method.

We estimate the fair value of our stock-based awards to employees and non-employees using the Black-Scholes option pricing model, which requires the input of highly subjective assumptions, including (1) the expected volatility of our stock, (2) the expected term of the award, (3) the risk-free interest rate and (4) expected dividends. Due to the lack of a public market for our common stock prior to the completion of our initial public offering in September 2013, and resulting lack of company-specific historical and implied volatility data, we have based our estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. For these analyses, we have selected companies with characteristics that we believe are comparable to ours, including enterprise value, risk profiles, position within the industry, and with historical share price information sufficient to meet the expected life of the stock-based awards. We compute the historical volatility data using the daily closing prices for the selected companies' shares during the equivalent period as the calculated expected term of our stock-based awards. We will continue to apply this process until a sufficient amount of historical

Table of Contents

information regarding the volatility of our own stock price becomes available. We have estimated the expected life of our employee stock options using the "simplified" method, whereby, the expected life equals the average of the vesting term and the original contractual term of the option. The risk-free interest rates for periods within the expected life of the option are based on the U.S. Treasury yield curve in effect during the period the options were granted.

We also estimate forfeitures at the time of grant, and revise those estimates in subsequent periods if actual forfeitures differ from estimates. We use historical data to estimate pre-vesting option forfeitures to the extent that actual forfeitures differ from our estimates, the difference is recorded as a cumulative adjustment in the period the estimates were revised. Stock-based compensation expense recognized in the financial statements is based on awards that are ultimately expected to vest.

We have computed the estimated fair value of stock options at the date of grant using the following weighted-average assumptions:

	Year Ended December 31,		Nine Months Ended September 30,	
	2011	**2012**	**2012**	**2013**
Expected volatility	66.0%	69.0%	66.9%	70.3%
Expected term (in years)	6.0	6.0	6.0	6.0
Risk-free interest rate	1.1%	0.9%	0.9%	1.4%
Expected dividend yield				

Stock-based compensation totaled approximately $1.2 million for the year ended December 31, 2012 and $1.4 million for the nine months ended September 30, 2013. As of September 30, 2013, we had $3.3 million of unrecognized compensation expense, net of related forfeiture estimates, which is expected to be recognized over a weighted-average remaining vesting period of approximately 2.2 years. We expect the impact of our stock-based compensation expense for stock-based awards granted to employees and non-employees to grow in future periods due to the potential increases in the value of our common stock and headcount.

The following table summarizes by grant date the number of shares of common stock underlying stock options granted from January 1, 2012 through the date we became a public company, as well as the associated per share exercise price and the retrospective estimated fair value per share of our common stock on the date of grant:

Date of Grant	**Number of Shares Subject to Awards**	**Exercise Price Per Share(1)**	**Retrospective Fair Value Per Share on Date of Grant(2)**
March 1, 2012	22,750	$ 5.28	$ 5.80
June 7, 2012	238,500	$ 5.28	$ 6.12
September 6, 2012	20,250	$ 5.28	$ 6.12
November 13, 2012	250,000	$ 5.28	$ 7.88
December 12, 2012	190,500	$ 7.12	$ 7.88
June 6, 2013	8,750	$ 9.64	n/a

(1) Due to the absence of a public market for our common stock prior to September 2013, the exercise price per share was the estimated fair value of common stock and represents the determination by our board of directors of the fair value of our common stock as of the date of each grant, taking into consideration various objective and subjective factors, as discussed more fully below.

Table of Contents

(2) The fair value of common stock at the grant date was adjusted in connection with a retrospective fair value assessment for financial reporting purposes, as discussed more fully below.

Determination of the Fair Value of Common Stock on Grant Dates

For grants made prior to the consummation of our initial public offering in September 2013, our audit committee recommended, and our board of directors determined, the fair value of our common stock considering, in part, the work of an independent third party valuation specialist. Due to the absence of a public market for our common stock, the board determined the estimated per share fair value of our common stock at various dates considering contemporaneous valuations performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants Practice Aid, *Valuation of Privately-Held Company Equity Securities Issued as Compensation*, also known as the Practice Aid. We engaged the valuation firm to perform contemporaneous valuations as of December 21, 2011, December 12, 2012, March 31, 2013 and June 6, 2013. In conducting the contemporaneous valuations, the valuation firm considered all objective and subjective factors that we believed to be relevant for each valuation conducted, including our best estimate of our business condition, prospects and operating performance at each valuation date. Within the contemporaneous valuations performed, a range of factors, assumptions and methodologies were used. The significant factors included:

- the prices of our preferred stock sold to or exchanged between outside investors in arm's length transactions, and the rights, preferences and privileges of our preferred stock as compared to those of our common stock, including the liquidation preferences of our preferred stock;
- our results of operations, financial position and the status of research and development efforts;
- the composition of, and changes to, our management team and board of directors;
- the lack of liquidity of our common stock;
- our stage of development and business strategy and the material risks related to our business and industry;
- the achievement of enterprise milestones, including entering into collaboration and license agreements;
- the valuation of publicly traded companies in the life sciences and biotechnology sectors, as well as recently completed mergers and acquisitions of peer companies;
- any external market conditions affecting the life sciences and biotechnology industry sectors;
- the likelihood of achieving a liquidity event for the holders of our common stock and stock options, such as an initial public offering, or IPO, or a sale of our company, given prevailing market conditions; and
- the state of the IPO market for similarly situated privately held biotechnology companies.

The dates of our contemporaneous valuations have not always coincided with the dates of our stock option grants. In determining the exercise prices of the stock options set forth in the table above, our board of directors considered, among other things, the most recent contemporaneous valuations of our common stock and our assessment of additional objective and subjective factors we believed were relevant as of the grant date. The additional factors considered when determining any changes in fair value between the most recent contemporaneous valuation and the grant dates included our stage of research and preclinical development, our operating and financial performance and current business conditions.

50

Table of Contents

There are significant judgments and estimates inherent in the determination of the fair value of our common stock. These judgments and estimates include assumptions regarding our future operating performance, the time to completing an IPO or other liquidity event, the related company valuations associated with such events, and the determinations of the appropriate valuation methods at each valuation date. If we had made different assumptions, our stock-based compensation expense, net income (loss) and net income (loss) per share applicable to common stockholders could have been different.

In early May 2013, based on the progress of our clinical pipeline, overall capital market conditions and the improving market for biopharmaceutical IPOs, our board of directors determined and directed management to begin preparation and submission of a confidential draft registration statement for an IPO. We selected underwriters and held an organizational meeting in June 2013. We believe these events increased the probability of an early IPO scenario and therefore in connection with the preparation of our financial statements for the year ended December 31, 2012, we retrospectively re-assessed the estimated fair value of our common stock for financial reporting purposes at interim dates between the contemporaneous valuations where there were stock option grants. For these interim periods, we adjusted the fair value based on market conditions, progress made in our development programs and whether we achieved company milestones.

Common Stock Valuation Methodologies

These contemporaneous and retrospective valuations were prepared in accordance with the guidelines in the Practice Aid, which prescribes several valuation approaches for setting the value of an enterprise, such as the cost, market and income approaches, and various methodologies for allocating the value of an enterprise to its common stock. We generally used the market approach, in particular the guideline company and precedent transaction methodologies, based on inputs from comparable public companies' equity valuations and comparable acquisition transactions, to estimate the enterprise value of our company.

Methods Used to Allocate Our Enterprise Value to Classes of Securities

In accordance with the Practice Aid, we considered the various methods for allocating the enterprise value across our classes and series of capital stock to determine the fair value of our common stock at each valuation date. The methods we considered consisted of the following:

Current Value Method. Under the current value method, once the fair value of the enterprise is established, the value is allocated to the various series of preferred and common stock based on their respective seniority, liquidation preferences or conversion values, whichever is greatest.

Option Pricing Method. Under the option pricing method, shares are valued by creating a series of call options with exercise prices based on the liquidation preferences and conversion terms of each equity class. The values of the preferred and common stock are inferred by analyzing these options.

Probability-Weighted Expected Return Method, or PWERM. The PWERM is a scenario-based analysis that estimates the value per share based on the probability-weighted present value of expected future investment returns, considering each of the possible outcomes available to us, as well as the economic and control rights of each share class.

We used the PWERM to allocate the enterprise values to the common stock for each valuation date. Under this method, the value of the common stock is estimated based upon an analysis of future values for our company assuming various investment outcomes, the timing of which is based, in part, on the plans of our board of directors and management. Under this approach, share value is derived from the probability-weighted present value of expected future investment returns, considering each of the

Table of Contents

possible outcomes available to us, as well as the economic and control rights of each share class. The fair value of our common stock was estimated using a probability-weighted analysis of the present value of the returns afforded to common stockholders under several future stockholder exit or liquidity event scenarios, either through (1) an IPO; (2) an acquisition or sale of our company at a premium to the cumulative liquidation preference of the preferred stockholders; or (3) a sale of our company at a value below the cumulative liquidation preference of the preferred stockholders.

The individual stockholder exit or liquidity scenarios considered in each analysis depended on the specific facts and circumstances, internal and external, present as of each valuation date. The future projected enterprise value used to value our common stock in the IPO scenarios and the sale scenarios were estimated by application of the market approach based on certain key assumptions, including the following:

- valuations of companies prior to the receipt of proceeds from initial public offerings completed within three years of the valuation date;
- estimated third-party sale values based on recent transactions involving biotechnology or biopharmaceutical companies; and
- expected dates for a future IPO or sale of our company.

The present values of our common stock under each scenario were then calculated by applying a risk-adjusted discount rate and then probability-weighting those present values based on our estimate of the relative probability of each scenario.

Finally, the estimated fair value of our common stock was reduced by a discount for lack of marketability. A discount is appropriate because our common stock is unregistered, and the holder of a minority interest in the common stock may not influence the timing of a liquidity event for our company. Our estimate of the appropriate discount for lack of marketability took into consideration put option methodologies consistent with the Practice Aid. We selected a smaller discount after taking into account empirical studies of restricted stock issued by publicly-traded companies.

March 1, 2012 Common Stock Valuation

We performed a retrospective valuation of our common stock as of March 1, 2012, and determined the fair value to be $5.80 per share as of that date. For the retrospective valuation at March 1, 2012, significant assumptions for the PWERM included the probability of occurrence of each scenario, timing to the liquidity event, discount rate and discount for lack of marketability. The specific facts and circumstances considered in assessing these key valuation assumptions included those noted in the following table:

March 1, 2012 Major Assumptions	IPO Short Term	IPO Long Term	Sale High	Sale Low	Sales Below Liquidation Preference
Probability of scenario	20%	20%	25%	25%	10%
Discount for lack of marketability			5%	5%	n/a
Timeline to liquidity (in years)	1.8	2.3	2.5	2.5	3.0
Discount rate common stock	30%	30%	30%	30%	n/a

In applying the market approach to estimate our future enterprise values under the IPO exit scenarios, as described previously, it was assumed that a liquidity event would occur in 1.8 years under a short term scenario or 2.3 years in the IPO long term scenario. We considered our development pipeline and our collaborations as of the valuation date. The selected enterprise value in the short-term scenario was based on the pre-money IPO market data for transactions between the third quartile and the maximum of the observed range. The selected aggregate enterprise value in the long-term scenario

Table of Contents

was based on consideration of the high-end of the observed range of transaction values and assumed our most advanced development projects would continue their positive clinical progression.

In applying the market approach to estimate our aggregate future enterprise values under the two sale scenarios, as described previously, it was assumed that a liquidity event would occur in 2.5 years for the high-case scenario and the low-case scenario. The selected enterprise value utilized in the low-case scenario considered the median of the observed range of comparable transaction values. The selected enterprise value for the high-case scenario was based on the comparable transaction values between the third quartile and the high-end of the observed range. We assumed we would make significant progress and achieve certain key milestones with respect to our development pipeline by the time a sale was consummated, including assumptions that our three most advanced development projects would continue their positive clinical progression, one or more additional compounds would enter Phase 1 trials and several other compounds would be nominated for pre-Investigational New Drug activities.

In the sale at a price below liquidation preference scenario, a sale of our existing research and intellectual property was assumed in 3.0 years, at a value that would not allow the preferred stockholders to realize their full liquidation preference resulting in no value to common stockholders.

Under all the exit scenarios considered in the PWERM, the fair value of our common stock was calculated using the estimated future enterprise valuations, a risk-adjusted discount rate of 30.0% based on the inherent risk of a hypothetical investment in our common stock, and a discount for lack of marketability which was 0% in the IPO scenarios and 5% in all other assumed liquidity events. The risk-adjusted discount rate was based on consideration of the weighted-average cost of capital for comparable biotechnology companies adjusted for company specific risk factors, the venture capital rates of return detailed in the Practice Aid, and an analysis of other quantitative and qualitative factors considered pertinent to estimating the discount rate. The resulting value, which represented the estimated fair value of our common stock as of March 1, 2012, was $5.80 per share.

June 7, 2012 and September 6, 2012 Common Stock Valuation

We performed a retrospective valuation of our common stock as of June 7, 2012, and determined the fair value to be $6.12 per share as of that date. For the retrospective valuation at June 7, 2012, significant assumptions for the PWERM included the probability of occurrence of each scenario, timing to the liquidity event, discount rate and discount for lack of marketability. The specific facts and circumstances in assessing these key valuation assumptions included those noted in the following table:

June 7, 2012 Major Assumptions	IPO Short Term	IPO Long Term	Sale High	Sale Low	Sales Below Liquidation Preference
Probability of scenario	25%	25%	25%	20%	5%
Discount for lack of marketability			5%	5%	n/a
Timeline to liquidity (in years)	1.5	2.0	2.5	2.5	3.0
Discount rate common stock	30%	30%	30%	30%	n/a

In applying the market approach to estimate our future enterprise values under the IPO exit scenarios, as described previously, it was assumed that a liquidity event would occur in 1.5 years under a short term scenario or 2.0 years in the IPO long term scenario. We considered our development pipeline and our collaborations as of the valuation date. The selected enterprise value in the short-term scenario was based on the pre-money IPO market data for transactions between the third quartile and the maximum of the observed range. The selected aggregate enterprise value in the long-term scenario was based on consideration of the high-end of the observed range of transaction values and assumed our most advanced development projects would continue their positive clinical progression.

Table of Contents

In applying the market approach to estimate our aggregate future enterprise values under the two sale scenarios, as described previously, it was assumed that a liquidity event would occur in 2.5 years for the high-case scenario and the low-case scenario. The selected enterprise value utilized in the low-case scenario considered the median of the observed range of comparable transaction values. The selected enterprise value for the high-case scenario was based on the comparable transaction values between the third quartile and the high-end of the observed range. We assumed we would make significant progress and achieve certain key milestones with respect to our development pipeline by the time a sale was consummated, including assumptions that our three most advanced development projects would continue their positive clinical progression, one or more additional compounds would enter Phase 1 trials and several other compounds would be nominated for pre-IND activities.

In the sale at a price below liquidation preference scenario, a sale of our existing research and intellectual property was assumed in 3.0 years, at a value that would not allow the preferred stockholders to realize their full liquidation preference resulting in no value to common stockholders.

Under all the exit scenarios considered in the PWERM, the fair value of our common stock was calculated using the estimated future enterprise valuations, a risk-adjusted discount rate of 30% based on the inherent risk of a hypothetical investment in our common stock, and a discount for lack of marketability which was decreased to 0% in the long-term IPO scenarios and remained 5% in all other assumed liquidity events. The risk-adjusted discount rate was based on consideration of the weighted-average cost of capital for comparable biotechnology companies adjusted for company specific risk factors, the venture capital rates of return detailed in the Practice Aid, and an analysis of other quantitative and qualitative factors considered pertinent to estimating the discount rate. The resulting value, which represented the estimated fair value of our common stock as of June 7, 2012, was $6.12 per share.

The estimated per share fair value of our common stock calculated in our valuation as of June 7, 2012 of $6.12 per share increased from the March 1, 2012 valuation of $5.80 per share primarily due to the following factors:

- timing to a prospective liquidity event had decreased; and
- likelihood of an IPO had increased.

As a result of the fact that the number of stock option grants were not significant on September 6, 2012, we utilized the June 7, 2012 valuation to determine the retrospective fair value of our common stock in September 2012.

November 13, 2012 and December 12, 2012 Common Stock Valuation

We performed a retrospective valuation of our common stock as of November 13, 2012, and determined the fair value to be $7.88 per share as of that date. For the retrospective valuation at November 13, 2012, significant assumptions for the PWERM included the probability of occurrence of each scenario, timing to the liquidity event, discount rate and discount for lack of marketability. The specific facts and circumstances considered in assessing these key valuation assumptions included those noted in the following table:

November 13, 2012 Major Assumptions	IPO Short Term	IPO Long Term	Sale High	Sale Low	Sales Below Liquidation Preference
Probability of scenario	30%	25%	25%	15%	5%
Discount for lack of marketability			5%	5%	n/a
Timeline to liquidity (in years)	1.0	1.5	2.0	2.0	2.5
Discount rate common stock	30%	30%	30%	30%	n/a

Table of Contents

In applying the market approach to estimate our future enterprise values under the IPO exit scenarios, as described previously, it was assumed that a liquidity event would occur in 1.0 years under a short term scenario or 1.5 years in the IPO long term scenario due to improvement in IPO market conditions for companies in our industry. We considered our development pipeline and our collaborations as of the valuation date. The selected enterprise value in the short-term scenario was based on the pre-money IPO market data for transactions between the third quartile and the maximum of the observed range. The selected aggregate enterprise value in the long-term scenario was based on consideration of the high-end of the observed range of transaction values and assumed our most advanced development projects would continue their positive clinical progression.

In applying the market approach to estimate our aggregate future enterprise values under the two sale scenarios, as described previously, it was assumed that a liquidity event would occur in 2.0 years for the high-case scenario and the low-case scenario. The selected enterprise value utilized in the low-case scenario considered the median of the observed range of comparable transaction values. The selected enterprise value for the high-case scenario was based on the comparable transaction values between the third quartile and the high-end of the observed range. We assumed we would make significant progress and achieve certain key milestones with respect to our development pipeline by the time a sale was consummated, including assumptions that our three most advanced development projects would continue their positive clinical progression, one or more additional compounds would enter Phase 1 trials and several other compounds would be nominated for pre-IND activities.

In the sale at a price below liquidation preference scenario, a sale of our existing research and intellectual property was assumed in 2.5 years, at a value that would not allow the preferred stockholders to realize their full liquidation preference resulting in no value to common stockholders.

Under all the exit scenarios considered in the PWERM, the fair value of our common stock was calculated using the estimated future enterprise valuations, a lower risk-adjusted discount rate of 25% based on a reduction in the inherent risk of a hypothetical investment in our common stock, and a discount for lack of marketability which remained 0% in the IPO scenarios and remained 5% in all other assumed liquidity events. The risk-adjusted discount rate was based on consideration of the weighted-average cost of capital for comparable biotechnology companies adjusted for company specific risk factors, the venture capital rates of return detailed in the Practice Aid, and an analysis of other quantitative and qualitative factors considered pertinent to estimating the discount rate. The resulting value, which represented the estimated fair value of our common stock as of November 13, 2012, was $7.88 per share.

The estimated per share fair value of our common stock calculated in our valuation as of November 13, 2012 of $7.88 per share increased from the June 7, 2012 retrospective valuation estimate of $6.12 per share primarily due to the following factors:

- timing to a prospective liquidity event has decreased since June 2012;
- increased likelihood of an IPO; and
- initiation of a Phase 2 clinical trial of dalantercept in endometrial cancer.

As a result of the fact that there were no material changes to our business from November 13, 2012 to December 12, 2012, we utilized the November 13, 2012 valuation to determine the exercise price of option grants in December.

March 31, 2013 Common Stock Valuation

We performed a contemporaneous valuation of our common stock as of March 31, 2013, and determined the fair value to be $8.68 per share as of that date. For the valuation at March 31, 2013, significant assumptions for the PWERM included the probability of occurrence of each scenario, timing

Table of Contents

to the liquidity event, discount rate and discount for lack of marketability. The specific facts and circumstances considered in assessing these key valuation assumptions included those noted in the following table:

March 31, 2013 Major Assumptions	IPO Short Term	IPO Long Term	Sale High	Sale Low	Sales Below Liquidation Preference
Probability of scenario	50%	10%	20%	15%	5%
Discount for lack of marketability			5%	5%	n/a
Timeline to liquidity (in years)	0.6	1.0	1.8	2.0	2.3
Discount rate common stock	25%	25%	25%	25%	n/a

In applying the market approach to estimate our future enterprise values under the IPO exit scenarios, as described previously, it was assumed that a liquidity event would occur in 7 months under a short term scenario and 1.0 years in the IPO long term scenario. We considered our development pipeline and our collaborations as of the valuation date. The selected enterprise value in the short-term scenario was based on the pre-money IPO market data for transactions between the third quartile and the maximum of the observed range. The selected aggregate enterprise value in the long-term scenario was based on consideration of the high-end of the observed range of transaction values and assumed our most advanced development projects would continue their positive clinical progression.

In applying the market approach to estimate our aggregate future enterprise values under the two trade sale scenarios, as described previously, it was assumed that a liquidity event would occur in 1.8 years for the high-case scenario and 2.0 years the low-case scenario. The selected enterprise value utilized in the low-case scenario considered the median of the observed range of comparable transaction values. The selected enterprise value for the high-case scenario was based on the comparable transaction values between the third quartile and the high-end of the observed range. We assumed we would make significant progress and achieve certain key milestones with respect to our development pipeline by the time a trade sale was consummated, including assumptions that our three most advanced development projects would continue their positive clinical progression, one or more additional compounds would enter Phase 1 trials and several other compounds would be nominated for pre-IND activities.

In the sale at a price below liquidation preference scenario, a sale of our existing research and intellectual property was assumed in 2.3 years, at a value that would not allow the preferred stockholders to realize their full liquidation preference resulting in no value to common stockholders.

Under all the exit scenarios considered in the PWERM, the fair value of our common stock was calculated using the estimated future enterprise valuations, a lower risk-adjusted discount rate of 25% based on a reduction to the inherent risk of a hypothetical investment in our common stock, and a discount for lack of marketability which remained at 0% in the IPO scenarios and remained 5% in all other assumed liquidity events. The risk-adjusted discount rate was based on consideration of the weighted-average cost of capital for comparable biotechnology companies adjusted for company specific risk factors, the venture capital rates of return detailed in the Practice Aid, and an analysis of other quantitative and qualitative factors considered pertinent to estimating the discount rate. The resulting value, which represented the estimated fair value of our common stock as of March 31, 2013, was $8.68 per share.

The estimated per share fair value of our common stock calculated in our valuation as of March 31, 2013 of $8.68 per share increased from the November 13, 2012 valuation of $7.88 per share primarily due to the following factors:

NASDAQ Biotechnology index increasing 20.8% from November 13, 2012 to March 31, 2013;

Table of Contents

improved capital market conditions for biotechnology companies as evidenced by a recent increase in the number of IPOs and their valuations;

increased likelihood of our board of directors recommending that we pursue an IPO;

decreased timing to a prospective liquidity event; and

initiation of several Phase 2 clinical trials for ACE-536 and dalantercept.

June 6, 2013 Common Stock Valuation

We performed a contemporaneous valuation of our common stock as of June 6, 2013, and determined the fair value to be $9.64 per share as of that date.

For the contemporaneous valuation at June 6, 2013, significant assumptions for the PWERM included the probability of occurrence of each scenario, timing to the liquidity event, discount rate and discount for lack of marketability. The specific facts and circumstances considered in assessing these key valuation assumptions included those noted in the following table:

June 6, 2013 Major Assumptions	IPO Short Term	IPO Long Term	Sale High	Sale Low	Sales Below Liquidation Preference
Probability of scenario	60%	10%	15%	10%	5%
Discount for lack of marketability			5%	5%	n/a
Timeline to liquidity (in years)	0.4	0.8	1.6	1.8	2.1
Discount rate common stock	25%	25%	25%	25%	n/a

In applying the market approach to estimate our future enterprise values under the IPO exit scenarios, as described previously, it was assumed that a liquidity event would occur in 5 months under a short term scenario and 10 months in the IPO long term scenario. We considered our development pipeline and our collaborations as of the valuation date. The selected enterprise value in the short-term scenario was based on the pre-money IPO market data for transactions between the third quartile and the maximum of the observed range. The selected aggregate enterprise value in the long-term scenario was based on consideration of the high-end of the observed range of transaction values and assumed our most advanced development projects would continue their positive clinical progression.

In applying the market approach to estimate our aggregate future enterprise values under the two trade sale scenarios, as described previously, it was assumed that a liquidity event would occur in 1.6 years for the high-case scenario and 1.8 years the low-case scenario. The selected enterprise value utilized in the low-case scenario considered the median of the observed range of comparable transaction values. The selected enterprise value for the high-case scenario was based on the comparable transaction values between the third quartile and the high-end of the observed range. We assumed we would make significant progress and achieve certain key milestones with respect to our development pipeline by the time a trade sale was consummated, including assumptions that our three most advanced development projects would continue their positive clinical progression, one or more additional compounds would enter Phase 1 trials and several other compounds would be nominated for pre-IND activities.

In the sale at a price below liquidation preference scenario, a sale of our existing research and intellectual property was assumed in 2.1 years, at a value that would not allow the preferred stockholders to realize their full liquidation preference resulting in no value to common stockholders.

Under all the exit scenarios considered in the PWERM, the fair value of our common stock was calculated using the estimated future enterprise valuations, a lower risk-adjusted discount rate of 25% based on a reduction to the inherent risk of a hypothetical investment in our common stock, and a discount for lack of marketability which remained at 0% in the IPO scenarios and remained 5% in all

Table of Contents

other assumed liquidity events. The risk-adjusted discount rate was based on consideration of the weighted-average cost of capital for comparable biotechnology companies adjusted for company specific risk factors, the venture capital rates of return detailed in the Practice Aid, and an analysis of other quantitative and qualitative factors considered pertinent to estimating the discount rate. The resulting value, which represented the estimated fair value of our common stock as of June 6, 2013, was $9.64 per share.

The estimated per share fair value of our common stock calculated in our valuation as of June 6, 2013 of $9.64 per share increased from the March 31, 2013 valuation of $8.68 per share primarily due to the following factors:

- timing to a prospective liquidity event has decreased since March 2013;
- NASDAQ Biotechnology (^NBI) index increasing 9.9% from April 1, 2013 to June 6, 2013;
- improved capital market conditions for biotechnology companies as evidenced by a recent increase in the number of public offerings and their initial public offering valuations;
- the occurrence of the organizational meeting for our potential IPO on June 5, 2013;
- received two FDA Orphan Designations for ACE-536; and
- initiated Phase 2 trial of ACE-536 in with β-thalassemia.

Initial public offering price

The initial public offering price of $15.00 per share was determined as a result of negotiations between us and the underwriters. In comparison, our estimate of the fair value of our common stock was $9.64 per share as of June 6, 2013. As is typical in initial public offerings, the initial public offering price was not derived using a formal determination of fair value, but was determined by negotiation between us and the underwriters. Among the factors that were considered in setting this price were the following:

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

The initial public offering price reflected a significant increase over the estimated valuation as of June 6, 2013 of $9.64 per share. We believe the difference is due to the following factors:

- The contemporaneous valuation prepared as of June 6, 2013 contained multiple liquidity scenarios, including an initial public offering with an anticipated completion date of mid-September 2013 to which we assigned a probability weighting of 60%. However, the consideration of different scenarios accounts for some but not all of the difference between the initial public offering price and the valuation as of June 6, 2013;

Advancement in the dose escalation phases of the on-going sotatercept and ACE-536 clinical trials in MDS and β-thalassemia;

Advancement in the treatment of patients in the on-going dalantercept clinical trials in renal cell carcinoma and squamous cell carcinoma of the head and neck;

Table of Contents

Improved capital market conditions for companies in our industry, as evidenced by a recent increase in the number of public offerings by such companies and in the initial public offering valuations of such companies compared to the valuations in their most recent pre-IPO equity financing;

The initial offering price necessarily assumed that the initial public offering had occurred, a public market for our common stock had been created and that our preferred stock had converted into common stock in connection with the initial public offering and, therefore, excluded the marketability or illiquidity discounts associated with the timing or likelihood of an initial public offering, the superior rights and preferences of our preferred stock and the alternative scenarios considered in the contemporaneous valuations over the past two years. Our June 6, 2013 valuation included an illiquidity discount of 0% in the IPO scenarios and 5% for the trade sale and liquidation scenarios;

In the public markets we believe there are investors who may apply more qualitative and subjective valuation criteria to certain of our clinical assets than the valuation methods applied in our valuations, although there can be no assurance that this will in fact be the case. As described above, as a private company we used a more quantitative methodology to determine the fair value of our common stock and this methodology differs from the methodology used to determine the initial public offering price. The initial public offering price was not derived using a formal determination of fair value, but rather was determined by negotiation between us and the underwriters. In particular, the estimate of fair value of our common stock as of June 6, 2013 was not a factor in setting the initial public offering price; and

The price that investors were willing to pay in the initial public offering may have taken into account other things that were not been expressly considered in our prior valuations, were not objectively determinable and that valuation models were not able to quantify.

There are significant additional judgments and estimates inherent in the determination of these valuations. These judgments and estimates include assumptions regarding our future performance, including the successful enrollment and completion of our clinical studies as well as the determination of the appropriate valuation methods. If we had made different assumptions, our stock-based compensation expense could have been different. The foregoing valuation methodologies are not the only methodologies available and they have not been used by us since the completion of our initial public offering. We cannot make assurances as to any particular valuation for our common stock. Accordingly, investors are cautioned not to place undue reliance on the foregoing valuation methodologies as an indicator of future stock prices.

Warrants to Purchase Preferred Stock and Common Stock

As of September 30, 2013, we had warrants outstanding to purchase 1,011,590 shares of common stock, of which warrants to purchase 857,586 shares of our common stock contain a provision requiring an adjustment to the number of shares in the event we issue common stock, or securities convertible into or exercisable for common stock, at a price per share lower than the warrant exercise price. The anti-dilution feature requires the warrants to be classified as liabilities and measured at fair value, with changes in fair value recognized as a component of other income (expense). The fair value of the warrants to purchase common stock on the date of issuance and on each re-measurement date for those warrants to purchase common stock are classified as liabilities and are estimated using the Monte Carlo simulation framework. The Company estimated that there would be up to three future financing events over the remaining life of the warrants to purchase common stock. Any modifications to the warrant liabilities are recorded in earnings during the period of the modification. The significant assumptions used in estimating the fair value of our warrant liabilities include the exercise price, volatility of the stock underlying the warrant, risk-free interest rate, estimated fair value of the stock underlying the warrant, and the estimated life of the warrant.

Table of Contents

Additionally, prior to the completion of our initial public offering in September 2013, we had warrants outstanding to purchase shares of Series B, Series C-1 and Series D-1 preferred stock. Freestanding warrants that are related to the purchase of redeemable preferred stock were classified as liabilities and recorded at fair value regardless of the timing of the redemption feature or the redemption price or the likelihood of redemption. The warrants were subject to re-measurement at each balance sheet date and any change in fair value was recognized as a component of other income (expense), net. We measured the fair value of our warrants to purchase preferred stock using a Black-Scholes option pricing model. In connection with the closing of our initial public offering on September 24, 2013, the outstanding warrants to purchase Series B Preferred Stock, Series C-1 Preferred Stock, and Series D-1 Preferred Stock were converted into warrants to purchase common stock and are now classified as a component of equity and are no longer subject to remeasurement. The exercise prices for each of these warrants remained unchanged.

Emerging Growth Company Status

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

Results of Operations

Comparison of the Nine Months Ended September 30, 2012 and 2013

(in thousands)	Nine Months Ended September 30, 2012	2013	Increase (Decrease)
Revenue:			
Collaboration revenue:			
License and milestone	$ 7,226	$ 36,044	$ 28,818
Cost-sharing, net	4,043	9,666	5,623
Total revenue	11,269	45,710	34,441
Costs and expenses:			
Research and development	25,646	25,834	188
General and administrative	6,318	9,472	3,154
Total costs and expenses	31,964	35,306	3,342
Income (loss) from operations	(20,695)	10,404	31,099
Other income (expense), net	(1,508)	(14,192)	(12,684)
Net income (loss)	$ (22,203)	$ (3,788)	$ 18,415

Revenue. We recognized revenue of $45.7 million in the nine months ended September 30, 2013, compared to $11.3 million in the same period in 2012. The $34.4 million increase was primarily due to the $10.0 million milestone payment received in connection with our Celgene collaboration for the first patient dosed in a Phase 2 trial in ACE-536 and recognizing an additional $18.6 million of deferred revenue because Shire ended our collaboration as of June 30, 2013. The remaining increase of $5.8 million was primarily due to an increase in net cost-sharing revenue from Celgene of $6.9 million due to Celgene assuming 100% of the costs of development for these protein therapeutic candidates as of January 1, 2013, and recognition of $0.2 million deferred revenue from Celgene, offset by a decrease

Table of Contents

in net cost-sharing revenue from Shire of $1.3 million due to the end of the collaboration as of June 30, 2013.

The following table shows revenue from all sources for the periods presented.

(in thousands)	Nine Months Ended September 30, 2012	2013	Increase (Decrease)
Collaboration revenue:			
Celgene:			
License and milestone	$ 1,491	$ 11,721	$ 10,230
Cost-sharing, net	2,106	8,961	6,855
Total Celgene	3,597	20,682	17,085
Shire:			
License and milestone	5,735	24,323	18,588
Cost-sharing, net	1,937	705	(1,232)
Total Shire	7,672	25,028	17,356
Total collaboration revenue	11,269	45,710	34,441
Total revenue	$ 11,269	$ 45,710	$ 34,441

Research and Development Expenses. Research and development expenses were $25.8 million in the nine months ended September 30, 2013, compared to $25.6 million in the same period in 2012. This $0.2 million increase was primarily due to an increase in expenses associated with clinical activity totaling $2.8 million, partially offset by a reduction in preclinical animal studies totaling $2.5 million.

General and Administrative Expenses. General and administrative expenses were $9.5 million in the nine months ended September 30, 2013, compared to $6.3 million in the same period in 2012. This $3.2 million increase was primarily related to higher professional fees for legal services in connection with our litigation with the Salk Institute and for increased professional fees and financial consulting services in connection with business development activities totaling $2.3 million and higher total compensation expenses totaling $0.9 million.

Other Expense, Net. Other expense, net was $14.2 million in the nine months ended September 30, 2013, compared to $1.5 million in the same period in 2012. This $12.7 million increase was primarily due to higher expense associated with the increase in fair value of the liability for warrants of $12.0 million and an increase in interest expense of $0.7 million due to a higher average outstanding debt balance in the first half of 2013.

Table of Contents

Comparison of Years Ended December 31, 2011 and 2012

(in thousands)	Year Ended December 31, 2011	2012	Increase (Decrease)
Revenue:			
Collaboration revenue:			
License and milestone	$ 74,406	$ 9,696	$ (64,710)
Cost-sharing, net	4,760	5,558	798
Contract manufacturing	1,745		(1,745)
Total revenue	80,911	15,254	(65,657)
Costs and operating expenses:			
Research and development	32,713	35,319	2,606
General and administrative	8,142	8,824	682
Cost of contract manufacturing revenue	1,500		(1,500)
Total costs and expenses	42,355	44,143	1,788
Income (loss) from operations	38,556	(28,889)	(67,445)
Other expense, net	(2,290)	(3,693)	(1,403)
Net income (loss)	$ 36,266	$ (32,582)	$ (68,848)

Revenue. We recognized revenue of $15.3 million for the year ended December 31, 2012, compared to $80.9 million for the year ended December 31, 2011. The $65.6 million decrease in revenue in 2012 was primarily due to a decrease of $64.7 million in license and milestone revenue, because during 2011, upon signing the ACE-536 Celgene collaboration and amending the sotatercept agreement, we recognized upfront payments and deferred revenue totaling $54.8 million. During 2011, we also recognized the remaining $2.4 million of deferred revenue from the Alkermes collaboration. Also, in 2012 we did not recognize any milestone payments compared to $7.0 million during 2011. The decrease in license and milestone revenue was offset by higher 2012 cost-sharing revenue due primarily to lower reimbursements paid to Shire for ACE-031. We also recognized $1.7 million for a contract manufacturing project during 2011.

Table of Contents

The following table shows revenue from all sources for the periods presented.

(in thousands)	Year Ended December 31, 2011	2012	Increase (Decrease)
Collaboration revenue:			
Celgene:			
License and milestone	$ 63,607	$ 2,035	$ (61,572)
Cost-sharing, net	(121)	2,879	3,000
Total Celgene	63,486	4,914	(58,572)
Shire:			
License and milestone	8,392	7,661	(731)
Cost-sharing, net	4,148	2,679	(1,469)
Total Shire	12,540	10,340	(2,200)
Alkermes:			
License and milestone	2,407		(2,407)
Cost-sharing, net	733		(733)
Total Alkermes	3,140		(3,140)
Total collaboration revenue	79,166	15,254	(63,912)
Contract manufacturing revenue	1,745		(1,745)
Total revenue	$ 80,911	$ 15,254	$ (65,657)

Research and Development Expenses. Research and development expenses were $35.3 million in the year ended December 31, 2012, compared to $32.7 million for the year ended December 31, 2011. This $2.6 million increase was primarily due to increases in expenses related to preclinical animal toxicology studies of $2.6 million, patent-related legal services of $0.9 million, external testing of $0.6 million, clinical trial activities of $0.5 million, contract labor of $0.5 million, outsourced research of $0.3 million and management bonuses of $0.3 million partially offset by decreases in expenses related to depreciation of $1.3 million, contract manufacturing of $0.7 million, supplies of $0.4 million, and in-licensing of $0.5 million.

General and Administrative Expenses. General and administrative expenses were $8.8 million in the year ended December 31, 2012, compared to $8.1 million for the year ended December 31, 2011. This $0.7 million increase was primarily related to higher professional fees for legal costs of $0.4 million in connection with litigation activities and higher compensation costs of $0.3 million.

Cost of Contract Manufacturing Revenue. There was no cost of contract manufacturing revenue for the year ended December 31, 2012, compared to $1.5 million for the year ended December 31, 2011. This decrease was due to there being no contract manufacturing services provided during 2012.

Other Expense, Net. Other expense, net was $3.7 million in the year ended December 31, 2012, compared to $2.3 million for the year ended December 31, 2011. The increase was primarily due to a $1.8 million increase in fair value of the liability for warrants to purchase redeemable convertible preferred stock and common stock.

Liquidity and Capital Resources

We have incurred losses and cumulative negative cash flows from operations since our inception in June 2003, and as of September 30, 2013, we had an accumulated deficit of $174.2 million. We anticipate that we will continue to incur losses for at least the next several years. We expect that our research and development and general and administrative expenses will continue to increase and, as a

Table of Contents

result, we will need additional capital to fund our operations, which we may raise through a combination of the sale of equity, debt financings or other sources, including potential additional collaborations.

As of September 30, 2013, our operations have been funded by $105.1 million in equity investments from venture investors, $49.2 million in equity investments from our partners, and $192.6 million in upfront payments, milestones, and net research and development payments from our partners.

In September 2013, we completed the sale of 6,417,000 shares of our common stock, including 837,000 shares of common stock sold pursuant to the underwriters' full exercise of their option to purchase additional shares at a public offering price of $15.00 per share, resulting in net proceeds to us of $86.8 million, after deducting underwriting discounts and offering expenses. Also in September 2013, we completed a private placement of $10 million of our common stock at a price of $15.00 per share.

As of September 30, 2013, we had $116.5 million in cash and cash equivalents. Cash in excess of immediate requirements is invested in accordance with our investment policy, primarily with a view to liquidity and capital preservation. Currently, our funds are held in money market mutual funds consisting of U.S. government-backed securities.

We entered into a new venture debt facility on June 7, 2012 and, as of September 30, 2013 we had $18.2 million in venture debt outstanding. After an interest-only period, we began paying down principal on the debt facility in July 2013. Interest accrues at a rate of 8.5% per annum and is payable monthly. The debt facility also included a closing fee of $0.2 million and is also subject to an additional deferred payment of $1.2 million which is due at the time of the final payment. We are amortizing the cost over the 42 months of the loan resulting in an effective interest rate of approximately 11.8%. We are not subject to any financial covenants and the debt facility is secured by a lien on all of our property as of, or acquired after, June 7, 2012, except for intellectual property. The debt facility matures in December 2015.

Cash Flows

The following table sets forth the primary sources and uses of cash for each of the periods set forth below:

	Year Ended December 31,		Nine Months Ended September 30,	
(in thousands)	**2011**	**2012**	**2012**	**2013**
Net cash provided by (used in):				
Operating activities	$ 9,056	$ (38,884)	$ (29,435)	$ (18,286)
Investing activities	(27)	(441)	(322)	(187)
Financing activities	21,092	13,899	13,801	95,341
Net increase (decrease) in cash and cash equivalents	$ 30,121	$ (25,426)	$ (15,956)	$ 76,868

Operating Activities. The significant decrease in net cash used in operating activities for the nine months ended September 30, 2013, compared to the nine months ended September 30, 2012, is primarily due to the receipt of a $10.0 million milestone payment from Celgene in the first quarter of 2013.The significant decrease in cash provided by operating activities for the year ended December 31, 2012, compared to the year ended December 31, 2011, is primarily due to the upfront and milestone payments of $32.5 million related to the ACE-536 Agreement received during 2011.

Net cash used in operating activities was $18.3 million for the nine months ended September 30, 2013, and consisted primarily of a net loss of $3.8 million adjusted for non-cash items including an increase in fair value of warrants of $12.6 million, stock-based compensation expense of $1.4 million,

Table of Contents

depreciation and amortization of $0.7 million, forgiveness of the related party receivable of $0.2 million, accretion of deferred interest of $0.3 million, and amortization of deferred debt issuance costs of $0.2 million, and a net decrease due to changes in operating assets and liabilities of $29.9 million. The significant items in the change in operating assets and liabilities include a decrease in deferred revenue of $26.0 million due primarily to the recognition of $24.3 million of deferred revenue for the Shire collaboration agreement which was terminated effective June 30, 2013. Other components of the change in operating assets and liabilities include a decrease in accrued expenses of $1.6 million, an increase in collaboration receivables of $1.3 million, an increase in prepaid expenses of $0.8 million, a decrease in deferred rent of $0.4 million and an increase in accounts payable of $0.2 million.

Net cash used in operating activities was $29.4 million for the nine months ended September 30, 2012 and consisted primarily of a net loss of $22.2 million adjusted for non-cash items including an increase in fair value of warrants of $0.6 million, stock-based compensation expense of $0.9 million, depreciation and amortization of $1.1 million, accretion of deferred interest of $0.3 million, and amortization of deferred debt issuance costs of $0.1 million, and a net decrease due to changes in operating assets and liabilities of $10.1 million. The significant items in the change in operating assets and liabilities include a decrease in deferred revenue of $7.2 million due to the ongoing recognition of revenue deferred in connection with up-front payments for the Celgene and Shire collaboration agreements, a decrease in accounts payable of $0.9 million and an increase in prepaid expenses and other current assets of $1.3 million. Other components of the change in operating assets and liabilities include an increase in collaboration receivables of $1.0 million, an increase in accrued expenses of $0.7 million and a decrease in deferred rent of $0.4 million.

Net cash used in operating activities was $38.9 million for the year ended December 31, 2012 and is primarily due to a net loss of $32.6 million adjusted for non-cash items including an increase in the fair value of warrants of $2.3 million, stock-based compensation of $1.2 million, depreciation and amortization of $1.3 million, and accretion of deferred interest of $0.3 million and a net decrease in operating assets and liabilities of $11.5 million. The significant items in the change in operating assets and liabilities include a decrease in deferred revenue of $9.7 million due to the ongoing recognition of revenue deferred in connection with up-front payments for the Celgene and Shire collaboration agreements, a decrease in accounts payable of $1.3 million and an increase in collaboration receivables of $1.1 million, offset in part by an increase in accrued expenses of $1.6 million. Other components of the change in operating assets and liabilities include an increase in prepaid expenses and other current assets of $0.6 million and a decrease in deferred rent of $0.5 million.

Net cash provided by operating activities was $9.1 million for the year ended December 31, 2011 and is primarily due to net income of $36.3 million, which was impacted by non-cash items including depreciation and amortization of $3.1 million, stock-based compensation of $1.4 million, an increase in the fair value of warrants of $0.5 million, accretion of deferred interest of $0.3 million and amortization of debt discount of $0.2 million and a net decrease in operating assets and liabilities of $32.8 million. The significant items in the change in operating assets and liabilities include a decrease in deferred revenue of $35.1 million due primarily to the acceleration of deferred revenue associated with the Celgene collaboration upfront payments as a result of the modification of the collaboration agreement, as well as a decrease in accrued expenses of $2.8 million, offset in part by a decrease in prepaid expenses and other current assets of $2.6 million and a decrease in collaboration receivables of $1.8 million. Other components of the change in operating assets and liabilities include an increase in accounts payable of $0.3 million and an increase in deferred rent of $0.2 million.

Investing Activities. Net cash used in investing activities was $0.2 million for the nine months ended September 30, 2013 and $0.3 million for the nine months ended September 30, 2012 and consisted of purchases of property and equipment.

Table of Contents

Net cash used in investing activities was $27,000 for the year ended December 31, 2011 and $0.4 million for the year ended December 31, 2012 and consisted of purchases of property and equipment.

Financing Activities. Net cash provided by financing activities was $95.3 million for the nine months ended September 30, 2013 and consisted of $97.4 million in net proceeds received from the company's initial public offering and concurrent private placement, offset by $1.8 million of principal payments made to pay down our venture debt line and $0.3 million paid to repurchase and retire redeemable convertible preferred stock, common stock and warrants to purchase common stock. Net cash provided by financing activities was $13.8 million for the nine months ended September 30, 2012 and consisted primarily of $19.9 million in net proceeds received from the drawdown of our new venture debt line in June 2012, offset by $6.2 million of principal payments made to pay down our previous venture debt line.

Net cash provided by financing activities was $21.1 million for the year ended December 31, 2011 and consisted primarily of $30.4 million of net proceeds received from the sale of 9,704,756 shares of our Series F preferred stock, as well as $0.2 million received from the exercise of stock options and warrants to purchase common stock, offset in part by $9.5 million of principal payments made to pay down a previous venture debt facility.

Net cash provided by financing activities was $13.9 million for the year ended December 31, 2012 and consisted of $19.9 million in net proceeds received from the drawdown of our new venture debt line in June 2012, as well as $0.2 million received from the exercise of stock options and warrants to purchase common stock, offset by $6.2 million of principal payments made to pay down our previous venture debt line.

Operating Capital Requirements

To date, we have not generated any revenue from product sales. We do not know when, or if, we will generate any revenue from product sales. We will not generate revenue from product sales unless and until we or our partners obtain regulatory approval of and commercialize one of our current or future protein therapeutics. We anticipate that we will continue to generate losses for the foreseeable future, and we expect the losses to increase as we continue the development of, and seek and obtain regulatory approvals for, dalantercept and any future protein therapeutics, and begin to commercialize any approved products. We are subject to all of the risks incident in the development of protein therapeutics, and we may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. Since the closing of our initial public offering, we have incurred, and expect to continue to incur, additional costs associated with operating as a public company. We anticipate that we will need additional funding in connection with our continuing operations.

We believe that the net proceeds we receive from this offering, together with receipt of anticipated milestone payments and our existing cash and cash equivalents will be sufficient to fund our projected operating requirements into the first quarter of 2017. However, we will require additional capital for the further development of our existing protein therapeutic candidates and may also need to raise additional funds sooner to pursue other development activities related to additional protein therapeutic candidates.

Until we can generate a sufficient amount of revenue from our products, if ever, we expect to fund our operations through a combination of equity offerings, or debt financings or other sources including potential additional collaborations. Additional capital may not be available on favorable terms, if at all. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of one or more of our protein therapeutic candidates. If we raise additional funds through the issuance of

Table of Contents

additional debt or equity securities, it could result in dilution to our existing stockholders and increased fixed payment obligations, and these securities may have rights senior to those of our common stock. If we incur indebtedness, we could become subject to covenants that would restrict our operations and potentially impair our competitiveness, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. We may not be able to enter into new collaboration arrangements for any of our proprietary protein therapeutic candidates. Any of these events could significantly harm our business, financial condition and prospects.

Our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement and involves risks and uncertainties, and actual results could vary as a result of a number of factors. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect. Our future funding requirements, both near and long-term, will depend on many factors, including, but not limited to:

- the achievement of milestones under our agreement with Celgene;
- the terms and timing of any other collaborative, licensing and other arrangements that we may establish;
- the initiation, progress, timing and completion of preclinical studies and clinical trials for our protein therapeutic candidates and potential protein therapeutic candidates;
- the number and characteristics of protein therapeutic candidates that we pursue;
- the progress, costs and results of our clinical trials;
- the outcome, timing and cost of regulatory approvals;
- delays that may be caused by changing regulatory requirements;
- the cost and timing of hiring new employees to support our continued growth;
- the costs involved in filing and prosecuting patent applications and enforcing and defending patent claims;
- the costs and timing of procuring clinical and commercial supplies of our protein therapeutic candidates;
- the extent to which we acquire or invest in businesses, products or technologies; and
- the costs involved in defending and prosecuting litigation regarding in-licensed intellectual property including our litigation with the Salk Institute. See "Business Litigation".

Table of Contents

Contractual Obligations and Commitments

The following is a summary of our long-term contractual cash obligations as of December 31, 2012.

(in thousands)	Total	Less than 1 Year	1 to 3 Years	3 to 5 Years	More than 5 Years
Operating lease obligations(1)	$ 23,979	$ 4,522	$ 8,628	$ 7,876	$ 2,953
Less: sublease income(2)	(1,407)	(583)	(824)		
Venture debt facility(3)	24,320	5,304	19,016		
Total	$ 46,892	$ 9,243	$ 26,820	$ 7,876	$ 2,953

(1) We lease office space at 128 Sidney Street and 149 Sidney Street in Cambridge, Massachusetts under noncancelable operating leases that expire in September 2018, and at 12 Emily Street in Cambridge, Massachusetts under a noncancelable operating lease that expires in May 2015.

(2) In February 2011, we entered into a sublease for 14,214 square feet of office space at 12 Emily Street in Cambridge, Massachusetts.

(3) In June 2012, we entered into a $20.0 million venture debt facility to provide working capital to fund operating activities. The loans under this debt facility are secured by our assets and are being repaid over 42 months beginning with a 12 month interest only period. Interest rates were fixed at the time of drawdown, with an effective rate of 11.8%.

We also have obligations to make future payments to third party licensors that become due and payable on the achievement of certain development, regulatory and commercial milestones. We have not included these commitments on our balance sheet or in the table above because the achievement and timing of these milestones is not fixed or determinable. These commitments include the following:

Under our license agreement with the Beth Israel Deaconess Medical Center, or BIDMC, in respect of BIDMC's joint interest in patent rights related to the treatment of renal cell cancer by combination therapy with dalantercept and VEGF-receptor tyrosine kinase inhibitors, we agreed to pay BIDMC specified development and sales milestone payments aggregating up to $1.0 million. In addition, we are required to pay BIDMC royalties in the low single digits on worldwide net product sales of drug labeled for treatment regimens that are claimed in the licensed patents.

Under our license agreement with the Ludwig Institute for Cancer Research, or LICR, in respect of patent rights relating to the first cloning of the type I activin receptors, as well as the treatment of pancreatic tumors with dalantercept, we agreed to pay LICR specified development and sales milestone payments aggregating up to $1.6 million relating to the development and commercialization of dalantercept. In addition, we are required to pay LICR royalties in the low single-digits on worldwide net product sales of dalantercept, with royalty obligations continuing at a 50% reduced rate for a period of time after patent expiration. If we sublicense the LICR patent rights, we will owe LICR a percentage of sublicensing revenue, excluding payments based on the level of sales, profits or other levels of commercialization.

Under our two license agreements with the Salk Institute for Biological Studies, or Salk, relating to the first cloning of the type II activin receptors, if we sublicense the Salk patent rights, we will owe Salk a percentage of sublicensing revenue, excluding payments based on sales. Under one agreement we also agreed to pay Salk specified development milestone payments totaling up to $2.0 million for sotatercept. Under the other agreement we also agreed to pay Salk specified development milestone payments of up to $0.7 million for ACE-536. In addition, under both agreements, we are required to pay Salk royalties in the low single-digits on worldwide net product sales by us or our sublicensees under the licensed patent rights of products claimed in

68

Table of Contents

the licensed patents, or products derived from use of the licensed patent rights, with royalty obligations for sotatercept continuing at a reduced rate for a period of time after patent expiration.

We enter into contracts in the normal course of business with CROs for clinical trials and clinical supply manufacturing and with vendors for preclinical safety and research studies, research supplies and other services and products for operating purposes. These contracts generally provide for termination on notice, and therefore are cancelable contracts and not included in the table of contractual obligations and commitments.

Net Operating Loss (NOL) Carryforwards

We have deferred tax assets of approximately $68.2 million as of December 31, 2012, which have been fully offset by a valuation allowance due to uncertainties surrounding our ability to realize these tax benefits. The deferred tax assets are primarily composed of federal and state tax net operating loss, or NOL, carryforwards and research and development tax credit carryforwards. As of December 31, 2012, we had federal NOL carryforwards of approximately $93.3 million and state NOL carryforwards of $75.4 million available to reduce future taxable income, if any. These federal NOL carryforwards expire at various times through 2032 and the state NOL carryforwards expire at various times through 2032. In general, if we experience a greater than 50 percent aggregate change in ownership of certain significant stockholders over a three-year period, or a Section 382 ownership change, utilization of our pre-change NOL carryforwards are subject to an annual limitation under Section 382 of the Internal Revenue Code of 1986, as amended, and similar state laws. Such limitations may result in expiration of a portion of the NOL carryforwards before utilization and may be substantial. If we experience a Section 382 ownership change in connection with this offering or as a result of future changes in our stock ownership, some of which changes are outside our control, the tax benefits related to the NOL carryforwards may be limited or lost.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined in the rules and regulations of the Securities and Exchange Commission.

Quantitative and Qualitative Disclosures About Market Risks

We are exposed to market risk related to changes in interest rates. As of September 30, 2013, we had cash and cash equivalents of $116.5 million. Our cash equivalents are invested in money market mutual funds consisting of U.S. government-backed securities. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments are in short-term securities. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our portfolio.

Table of Contents

BUSINESS

Overview

We are a clinical stage biopharmaceutical company focused on the discovery, development and commercialization of novel protein therapeutics for cancer and rare diseases. Our research focuses on the biology of the Transforming Growth Factor-Beta (TGF-β) protein superfamily, a large and diverse group of molecules that are key regulators in the growth and repair of tissues throughout the human body. We are leaders in understanding the biology of the TGF-β superfamily and in targeting these pathways to develop important new medicines. By coupling our discovery and development expertise, including our proprietary knowledge of the TGF-β superfamily, with our internal protein engineering and manufacturing capabilities, we have built a highly productive discovery and development platform that has generated innovative protein therapeutic candidates with novel mechanisms of action. These differentiated protein therapeutic candidates have the potential to significantly improve clinical outcomes for patients with cancer and rare diseases.

We focus on discovering and developing protein therapeutics that target a group of approximately 30 secreted proteins, or ligands, that are collectively referred to as the TGF-β superfamily. These ligands bind to subsets of 12 different receptors on the surface of cells, triggering intra-cellular changes in gene expression that guide cell growth and differentiation. The TGF-β superfamily ligands and their receptors represent an under-explored and diverse set of drug targets with the potential to yield therapeutics that modulate the growth and repair of diseased cells and tissues.

We have three internally discovered protein therapeutic candidates that are currently being studied in numerous ongoing Phase 2 clinical trials, focused on cancer and rare diseases. Our two most advanced protein therapeutic candidates, sotatercept and ACE-536, promote red blood cell production through a novel mechanism. Together with our collaboration partner, Celgene Corporation, we are developing sotatercept and ACE-536 to treat anemia and associated complications in patients with β-thalassemia and myelodysplastic syndromes (MDS). These red blood cell disorders are generally unresponsive to currently approved drugs. Our third clinical stage protein therapeutic candidate, dalantercept, is designed to inhibit blood vessel formation through a mechanism that is distinct from, and potentially synergistic with, the dominant class of cancer drugs that inhibit blood vessel formation, the vascular endothelial growth factor (VEGF) pathway inhibitors. We are developing dalantercept primarily for use in combination with these products to produce better outcomes for cancer patients. We estimate that we have spent approximately $142.1 million on research and development from 2010 through September 30, 2013.

Sotatercept and ACE-536 have already shown promising biological activity in our initial clinical trials. We and Celgene have conducted six human clinical trials with sotatercept in over 160 healthy volunteers and cancer patients. We have conducted one clinical trial with ACE-536 in healthy volunteers. In these studies, both sotatercept and ACE-536 caused a dose-dependent increase in the number of red blood cells. Based on these results, we and Celgene have initiated Phase 2 clinical trials with each of these protein therapeutic candidates in β-thalassemia and MDS. In the ongoing trials of sotatercept and ACE-536 in patients with β-thalassemia, we have observed encouraging, dose-dependent increases in hemoglobin in non-transfusion dependent patients at the three dose levels tested. We and Celgene plan to initiate Phase 3 clinical trials for one or both of these protein therapeutic candidates in one or both of β-thalassemia and MDS by the end of 2014 or early 2015.

With respect to our third clinical stage protein therapeutic candidate, dalantercept, we have conducted a single agent Phase 1 clinical trial in patients with advanced solid tumors. Of the 29 evaluable patients treated in this clinical trial, one had a partial response and 13 had stable disease, according to RECIST criteria. Additionally, we have studied the single agent activity of dalantercept in a Phase 2 clinical trial in patients with advanced head and neck cancer. Of the 29 evaluable patients at the 1.2 mg/kg dose level in this Phase 2 clinical trial, one had a partial response and ten had stable disease, according to RECIST criteria. Our ongoing focus is on the use of dalantercept in combination

Table of Contents

with an approved VEGF pathway inhibitor where we have provided both a mechanistic rationale and supportive preclinical data demonstrating dalantercept in combination with a VEGF pathway inhibitor provides enhanced anti-tumor effects in mice bearing human renal cell carcinoma xenographs. In an ongoing Phase 2 clinical trial of dalantercept in combination with axitinib, an approved VEGF pathway inhibitor, in patients with advanced renal cell carcinoma we have completed the dose escalation stage and found that dalantercept administered at a dose level of 1.2 mg/kg is well tolerated in combination with the FDA approved dose level of axitinib. We have now initiated the dose expansion phase of this study and plan to start the randomized controlled part of the study at the end of Q1 or early Q2 2014. We also intend to initiate a Phase 2 clinical trial of dalantercept in combination with the VEGF pathway inhibitor sorafenib in patients with liver cancer in the first half of 2014.

In addition to our clinical stage programs, we are developing a novel protein therapeutic candidate, ACE-083, for a first-in-human clinical trial that we expect to initiate by the end of 2014. ACE-083 has been designed to promote muscle growth in those muscles in which the drug is injected, with minimal systemic effect. We are focused on the development of ACE-083 for diseases in which increases in the size and function of specific muscles may provide a clinical benefit, including inclusion body myositis, facioscapulohumeral dystrophy (FSHD) and disuse atrophy.

We are developing sotatercept and ACE-536 through our exclusive worldwide collaborations with Celgene. As of January 1, 2013, Celgene became responsible for paying 100% of worldwide development costs for both programs. We may receive up to an additional $560.0 million of potential development, regulatory and commercial milestone payments and, if these protein therapeutic candidates are commercialized, we will receive a royalty on net sales in the low-to-mid 20% range. We will co-promote sotatercept and ACE-536, if approved, in North America for which our commercialization costs will be entirely funded by Celgene.

We have not entered into a partnership for dalantercept and retain worldwide rights to this program.

As of September 30, 2013, our operations have been funded primarily by $105.1 million in equity investments from venture investors, $86.8 million from investors in our initial public offering, $49.2 million in equity investments from our collaboration partners Celgene and Alkermes, Inc. ("Alkermes") and $192.6 million in upfront payments, milestones, and net research and development payments from our collaboration partners.

Our Strategy

Our goal is to be a leader in the discovery, development and commercialization of novel protein therapeutics for cancer and rare diseases. Key components of our strategy are:

Advance sotatercept and ACE-536 into Phase 3 trials in collaboration with Celgene. We and Celgene are jointly developing sotatercept and ACE-536. Assuming successful completion of the ongoing Phase 2 clinical trials in β-thalassemia and MDS, we plan to initiate Phase 3 clinical trials with Celgene for one or both protein therapeutics in one or both diseases by the end of 2014 or early 2015.

Explore new indications for sotatercept and ACE-536 with Celgene. We and Celgene are continuing our preclinical research to assess the opportunity for sotatercept and ACE-536 to treat certain red blood cell disorders known as hemoglobinopathies, which include diseases such as thalassemias and sickle cell disease. Based on our encouraging preclinical and clinical data in β-thalassemia and our emerging understanding of the mechanism of action of these protein therapeutic candidates, we believe there is a potential for activity for sotatercept and ACE-536 in sickle cell disease, and we continue to explore development of these protein therapeutic candidates for this disease.

Advance dalantercept into Phase 3-enabling clinical trials. Beyond our ongoing Phase 2 clinical trials, in 2014, we plan to initiate additional clinical trials of dalantercept in combination with

Table of Contents

either an approved anti-angiogenesis agent or chemotherapy in advanced solid tumors. One of these trials is expected to be in patients with liver cancer and other trials may be in patients with brain cancer, lung cancer or colon cancer.

Utilize our discovery and development platform to develop additional protein therapeutic candidates. In addition to sotatercept, ACE-536 and dalantercept, all of which were internally discovered using our research and development platform, we intend to continue to discover and develop other protein therapeutics that target and regulate various pathways in the TGF-β superfamily. We plan to bring an additional protein therapeutic candidate, ACE-083, into the clinic in 2014 targeting diseases involving muscle loss. We are also conducting pre-clinical development of ALK1 pathway inhibitors distinct from dalantercept for the treatment of diseases of the eye including age-related macular degeneration. In addition we are developing new protein therapeutic candidates for the treatment of cancer and diseases involving fibrosis.

Strategically leverage collaborations to advance our protein therapeutic candidates. To date, we have received more than $250.0 million from our corporate partners, including Celgene. Our two collaborations with Celgene for sotatercept and ACE-536 provide us with significant funding and access to Celgene's considerable scientific, development, regulatory and commercial capabilities. We will continue to strategically evaluate possible collaborations where doing so could enhance the development or commercialization of other protein therapeutic candidates in our pipeline.

Establish commercialization and marketing capabilities in North America and potentially other markets. We have retained co-promotion rights in North America for sotatercept and ACE-536, which will be entirely funded by Celgene. We intend to build hematology, oncology and neuromuscular disorder focused specialty sales forces and marketing capability to commercialize our protein therapeutic candidates that receive regulatory approval.

The Acceleron Discovery Platform: Novel Approaches to Potent Biology

Since our founding, we have focused on developing protein therapeutics that target a group of approximately 30 secreted proteins, or ligands, that are collectively referred to as the TGF-β superfamily. These ligands bind to subsets of 12 different receptors on the surface of cells, triggering intra-cellular changes in gene expression that guide cell growth and differentiation. The TGF-β superfamily ligands and their receptors represent a diverse and underexplored set of drug targets with the potential to yield potent therapeutics for the growth and repair of diseased cells and tissues. Applying our proprietary discovery and development platform, including our knowledge of the biology of the TGF-β superfamily and its receptors, we have generated a robust pipeline of innovative clinical and preclinical protein therapeutic candidates targeting key mechanisms underlying cancer and rare diseases.

Our Focus The TGF-β Superfamily

On a daily basis, the human body must orchestrate the growth and differentiation of cells to maintain and repair its cells and organ systems. Stem cells and precursor cells are undifferentiated cell types that reside in most tissues of the body. When tissue growth or regeneration is required, these undifferentiated cells divide and, through a series of intermediate stages, give rise to new, fully differentiated cells that build or repair the affected tissue. Decades of research have identified the TGF-β superfamily and its associated receptors as key regulators of the growth and differentiation of stem and precursor cells.

Until recently, regulation of the erythropoietin pathway was the primary therapeutic approach to stimulate red blood cell formation. Members of the TGF-β superfamily are now recognized as important regulators of red blood cell formation. We have shown that inhibition of members of the TGF-β superfamily ameliorates anemia in mouse models of β-thalassemia and MDS. Based on our findings, we are developing two protein therapeutic candidates, sotatercept and ACE-536, each of which is currently in Phase 2 clinical trials to treat patients with these diseases.

Table of Contents

Members of the TGF-β superfamily also play a significant role in regulating blood vessel formation. We and our academic collaborators have shown that mice with a genetic defect in a particular receptor for members of the TGF-β superfamily are resistant to tumor growth due to reduced blood vessel formation in the tumor. We have used this insight to design our Phase 2 anti-angiogenic agent, dalantercept, for the treatment of cancer.

Members of the family are also significant regulators of muscle development. A genetic defect in a TGF-β superfamily ligand, known as myostatin, causes profound increases in skeletal muscle. A naturally occurring mutation in myostatin has been identified in animals, such as "double-muscled" breeds of cattle and in the "bully whippet" offspring of whippet racing dogs, which have been selectively bred to have increased muscle mass or function. Furthermore, a mutation in myostatin has been identified in a human family, members of which exhibit exceptional musculature and strength. We are actively working on preclinical programs to increase muscle mass and strength.

Ligands of the TGF-β superfamily cause these profound biological effects by altering gene expression in target cells. As shown in the illustration below, a ligand of the superfamily initiates intracellular signaling by binding to a receptor that is located on the surface of a target cell. Upon binding to the ligand, the receptor activates specific transcription factors inside the target cell, which are called Smad proteins. The activated Smad proteins regulate gene expression and guide cellular growth and differentiation.

The TGF-β superfamily ligands are divided into subgroups termed the activins, the Growth and Differentiation Factors (GDFs), the Bone Morphogenetic Proteins (BMPs) and the TGF-β subgroup (for which the superfamily is named). Our clinical stage protein therapeutic candidates focus on the activin, GDF and BMP subgroups.

We believe that, by employing our proprietary discovery and development platform, we can design protein therapeutic candidates that alter TGF-β superfamily signaling and unlock the therapeutic potential of this group of proteins.

Acceleron Approach

By combining the powerful biology of the TGF-β superfamily with our discovery and development expertise and our internal protein engineering and manufacturing capabilities, we have built a robust clinical and preclinical pipeline of protein therapeutic candidates targeting key mechanisms underlying cancer and rare diseases.

We have taken a comprehensive, receptor-focused approach to access the biology of the TGF-β superfamily. We recognized that the 12 receptors for the superfamily act as control points for the ligands and therefore represent an attractive approach for pharmacological intervention. We have in-licensed patent rights for nine of the 12 receptors and systematically evaluated interactions between each receptor and a comprehensive panel of ligands. In the body, these ligands are naturally regulated by trap proteins that bind to the ligands thereby blocking ligand-receptor interactions and diminishing signaling in the cell. To mimic this natural regulatory approach, we have built our protein therapeutic

Table of Contents

candidates using the ligand-binding part of the receptors, depicted in the upper part of the figure below, as traps that capture the relevant groups of ligands in each biological process. We link the ligand-binding portion, the extracellular domain, of these receptors to the portion of a human antibody known as the Fc domain, depicted in the lower part of the figure below, which confers favorable pharmaceutical properties. The resulting "fused" proteins can be administered by simple intravenous or subcutaneous injection and reside in the blood for sufficient periods of time to permit dosing on a weekly or monthly basis.

Protein therapeutics constructed this way are referred to as "receptor fusion proteins" or "ligand traps". Some of the most successful protein therapeutics on the market belong to this category including Enbrel® (etanercept), Eylea® (aflibercept) and Orencia® (abatacept).

As shown in the figure below, our receptor fusion proteins act as ligand traps by binding to ligands of the TGF-β superfamily, preventing those ligands from binding to the cell surface receptors, and thereby preventing activation of Smad proteins in the target cell.

To take full advantage of our proprietary discovery and development platform, we have developed an integrated set of technologies and capabilities to rapidly and cost-effectively create, test and advance multiple protein therapeutic candidates. Our protein engineering expertise allows us to create and optimize our receptor fusion proteins. We have developed the capability to generate recombinant cell lines that produce our protein therapeutic candidates, and assess the activity of these molecules in

74

Table of Contents

animals using our internal animal pharmacology facility or the capabilities of our academic collaborators. We have also invested in infrastructure to manufacture Phase 1 and Phase 2 clinical material quickly and flexibly using our internal current good manufacturing practices, or cGMP, compliant protein production facility to support clinical development of our protein therapeutic candidates.

We use our integrated platform of research, development and manufacturing technologies to rapidly and cost-effectively create, test and advance our protein therapeutic candidates. Our robust clinical and preclinical pipeline is focused on areas of high-unmet medical need, particularly in the areas of cancer and rare diseases.

Our Product Pipeline

We have four development stage protein therapeutic candidates, of which three are currently in numerous ongoing clinical trials and the fourth we expect to begin human clinical trials by the end of 2014. Celgene is currently conducting four Phase 2 clinical trials and overseeing three investigator-sponsored trials with sotatercept. We are conducting two Phase 2 clinical trials with ACE-536, two Phase 2 clinical trials with dalantercept and overseeing a collaborative group-sponsored Phase 2 clinical trial of dalantercept. We expect to initiate a Phase 2 clinical trial with dalantercept in patients with hepatocellular carcinoma in the first half of 2014 and to initiate a Phase 1 clinical trial with ACE-083 by the end of 2014.

Sotatercept and ACE-536

Anemia in Patients with β-thalassemia and MDS

Erythropoiesis, the process by which precursor cells proliferate and differentiate to give rise to red blood cells, is one of the most important and active processes in human biology. The primary role of red blood cells is to carry and deliver oxygen to other cells throughout the body. At any given time, there are approximately 25 trillion red blood cells in normal adult circulation which account for roughly 25% of the body's total number of cells. The human body produces 2.4 million new red blood cells each second. Red blood cell formation starts in the bone marrow with cells referred to as red blood cell precursors. These precursor cells go through many rounds of cellular proliferation, combined with cellular differentiation, to become more specialized cells to carry out their role as mature, functional red blood cells. We believe this highly active process of red blood cell production is normally tightly controlled by positive and negative regulators of the erythropoietic process. Erythropoietin is a positive regulator that stimulates proliferation of early red blood cell precursor cells, the BFU-E and CFU-E

Table of Contents

cells depicted in the figure below. Based on our research, it is now recognized that certain ligands in the TGF-β superfamily are negative regulators of red blood cell precursors, starting with the Pro-E cells and those that follow, as depicted in the figure below. These members of the TGF-β superfamily restrain the maturation of these precursors into later stage precursors and ultimately into functional red blood cells (RBCs).

Depiction of Normal Erythropoiesis

In certain diseases, the highly active process of red blood cell production does not function properly, leading to a reduction in the number of functional red blood cells, a condition known as anemia. Anemia in some disease settings is currently treated by the use of erythropoiesis stimulating agents, such as recombinant erythropoietin, that stimulate proliferation of early stage precursors of red blood cells. However, in certain diseases, such as β-thalassemia and MDS, anemia is caused by defects in the production of late stage red blood cell precursors, which is known as ineffective erythropoiesis.

Anemias caused by ineffective erythropoiesis are not well-treated by current therapies. As shown in the illustration below, ineffective erythropoiesis is characterized by an over-abundance of early stage red blood cell precursors and a decreased ability of late stage precursor cells to properly differentiate into healthy, functional red blood cells. The resulting anemia stimulates the body's overproduction of erythropoietin, which exacerbates the over-abundance of early stage precursors. Because the defective step in ineffective erythropoiesis lies downstream of the early stage precursors, the increase in the number of these cells fails to resolve the anemia.

Depiction of Ineffective Erythropoiesis

76

Table of Contents

Based on our preclinical research, we believe that TGF-β superfamily ligands function as negative regulators of erythropoiesis by inhibiting the maturation of these early stage red blood cell precursors. Both sotatercept and ACE-536 are ligand traps designed to inhibit these negative regulators of late stage red blood cell precursors and promote their maturation into functional red blood cells.

We are developing sotatercept and ACE-536, through our collaborations with Celgene, as treatments for anemia in diseases in which erythropoiesis-stimulating agents are either not approved or are not well-suited to treat the underlying anemia. In diseases such as β-thalassemia and MDS in which anemia is caused by ineffective erythropoiesis, we believe both sotatercept and ACE-536 may help correct this defective process. Although similar in terms of their effects on red blood cells, there are differences in how these two protein therapeutic candidates bind to and inhibit ligands. Unlike ACE-536, sotatercept binds to and inhibits activin A, a TGF-β superfamily ligand, and has been shown to increase bone mass and biomarkers of bone formation in clinical trials. Given its effects on bone, sotatercept is being studied in patients with chronic kidney disease, where it has the potential to treat both anemia and mineral and bone disorder. In addition, in preclinical studies, sotatercept inhibits the growth of myeloma cells. Therefore, sotatercept is also being studied in multiple myeloma patients to inhibit tumor growth and improve the anemia and the bone loss associated with the disease.

β-thalassemia

The thalassemias comprise a heterogeneous group of disorders arising from defects in the genes that encode the proteins that comprise hemoglobin. Hemoglobin is a four-subunit protein complex formed of two α-subunits and two β-subunits, each with an iron-containing heme group that binds to and carries oxygen molecules within red blood cells. There are two main classifications of thalassemia, α-thalassemia and β-thalassemia, depending on whether the genetic defect lies in the gene encoding the α-subunit or the β-subunit. β-thalassemia is particularly prevalent throughout the Mediterranean region, Middle East, and Southeast Asia, and, due to migration and immigration, is now a global disease. The Thalassaemia International Federation estimates that there are approximately 300,000 patients worldwide with β-thalassemia, approximately 20,000 of which are in the United States and Europe, who are dependent on frequent blood transfusions. We estimate that there are at least as many β-thalassemia patients in the same regions who are not transfusion dependent and not included in these estimates. Many of these patients have hemoglobin levels that are approximately half that of normal individuals and experience significant complications of the disease.

Anemia of β-thalassemia is primarily a result of ineffective erythropoiesis. The genetic defect leads to decreased production of the β-subunits of hemoglobin resulting in an excess amount of the α-subunits. In normal erythropoiesis, excess unpaired α-subunits are eliminated by a cellular component called the proteasome. The proteasome is normally required for effective red blood cell maturation to selectively remove cellular components and organelles such as mitochondria which are replaced by hemoglobin, which constitutes 90% of the protein in a mature red blood cell. In thalassemia, the proteasome becomes saturated with the abnormally high levels of unpaired α-subunits and is unable to remove other cellular components and participate in the maturation process; this causes the block in maturation. Moreover, those free α-subunits that are not eliminated by the proteasome form aggregates, called hemichromes, which damage the maturing red blood cells. These hemichromes, along with the saturation of the proteasome by unpaired α-subunits, contribute to the ineffective erythropoiesis of β-thalassemia. The damaged red blood cells are filtered out by the spleen and have a reduced life span, resulting in anemia and enlargement of the spleen.

Patients with the most severe form of β-thalassemia produce few, if any, β-subunits, resulting in an increased amount of free α-subunits and consequently a high number of hemichromes. These patients typically present with life-threatening anemia within the first year of life and require regular and lifelong red blood cell transfusions, usually every 2 to 4 weeks. Because red blood cells contain significant amounts of iron, this intensive transfusion regimen contributes to a condition known as iron

Table of Contents

overload, which is the principal cause of mortality. Consequently, therapy to reduce iron overload, called iron chelation therapy, is also part of standard treatment in these patients and typically begins after patients have received approximately 20 transfusions during their lifetime. Iron chelation therapy alone costs between $25,000 and $40,000 per year and yet does not treat the underlying anemia. The course of the disease depends largely on whether patients are maintained on an adequate transfusion and iron chelation regimen. Poor compliance with transfusion and/or iron chelation is associated with a poor prognosis and shortened survival. However, even with the standard of care, patients are at risk of infection from transfusions as well as toxicities related to iron chelation therapy.

Patients with an intermediate form of β-thalassemia, who are not necessarily dependent on frequent transfusions early in life, nevertheless suffer from a wide range of debilitating conditions. The ongoing ineffective erythropoiesis leads to various complications affecting a wide range of organ systems. By the second decade of life, most of these patients' hemoglobin levels have declined to the 6-8 g/dL range, or approximately half that of normal individuals. In an attempt to correct this chronic anemia, the body produces high levels of erythropoietin resulting in a continued stimulation of the early red blood cell precursors in the bone marrow. The number of these precursors grows to such an extent in the bone marrow that it leads to skeletal deformities, porosity of the long bones, and bone fractures. Splenomegaly, or enlargement of the spleen, is the result in part of continuous clearance by the spleen of the malformed red blood cells damaged by hemichromes. This commonly leads patients to require removal of their spleen, which in turn leads to worsening of other complications, such as blood clots. Iron overload is another significant complication even in the absence of red blood cell transfusions. This is due to increased intestinal iron absorption as a result of the ongoing ineffective erythropoiesis. Patients also suffer from various endocrine disorders due, in large part, to the accumulation of iron in the endocrine glands. Importantly, iron can also accumulate in the liver and heart, leading to severe complications such as liver fibrosis and heart failure.

No drug is approved to treat the anemia of β-thalassemia. Hematopoietic stem cell transplantation is viewed as the only curative approach for β-thalassemia, although this option is limited by the availability of appropriate donors and by risks, including death, associated with the bone marrow transplant procedure. Consequently this treatment is used only in the most severely affected patients.

Myelodysplastic Syndromes

Myelodysplastic syndromes, or MDS, are a group of heterogeneous hematologic diseases characterized by abnormal proliferation and differentiation of blood precursor cells, including red blood cell precursors, in the bone marrow. This leads to peripheral reductions in red blood cells, often accompanied by decreases in white blood cells and platelets, as well as a risk of disease progression to acute myeloid leukemia. Anemia is present in the vast majority of MDS patients at the time of diagnosis. MDS is primarily a disease of the elderly, with 88% of cases diagnosed in individuals 60 years of age or older. Cancer surveillance databases estimate the annual incidence of MDS in the United States at 10,000 to 15,000 cases and the overall U.S. prevalence at approximately 30,000 to 60,000 patients.

Hematopoietic stem cell transplantation represents the only treatment modality with curative potential, although the relatively high morbidity and mortality of this approach limits its use. Approximately 23% of MDS patients are categorized as intermediate-2 to high risk. These patients are typically treated with inhibitors of DNA methyltransferase such as Vidaza® (2012 U.S. sales of $324 million for MDS) or Dacogen® (2012 U.S. sales of $233 million for MDS). Of the remaining 77% of patients categorized as low to intermediate-1 risk, approximately 10% have a specific chromosomal mutation and are typically treated with Revlimid® (2012 U.S. sales of $257 million for MDS). The remaining 67% of patients typically receive red blood cell transfusions or erythropoiesis stimulating agents, though erythropoiesis stimulating agents are not approved by the FDA or the EMA for the

Table of Contents

treatment of anemia in MDS patients. Our internal market research estimates that erythropoiesis stimulating agents generate $500 to $700 million in annual U.S. sales from their use in this disease.

The anemia in MDS is primarily due to ineffective erythropoiesis, and a significant number of MDS patients have serum erythropoietin levels substantially above the normal range, indicating that the anemia in these MDS patients is not a consequence of erythropoietin deficiency. The ineffective erythropoiesis of MDS may be caused by excess signaling by members of the TGF-β superfamily, which signaling inhibits red blood cell maturation. For this reason we believe that blocking this excess signaling by sotatercept or ACE-536 may reverse this inhibition. Approximately 50% of MDS patients are unresponsive to the administration of recombinant erythropoietin and instead require red blood cell transfusions, which can increase the risk of infection and iron-overload related toxicities. Treatment-resistant anemia resulting from ineffective erythropoiesis is a major cause of morbidity in MDS patients.

Chronic Kidney Disease

Anemia is a common complication of chronic kidney disease. Because erythropoietin is produced primarily in the kidney and to a lesser extent in the liver, patients with chronic kidney disease produce sub-optimal amounts of erythropoietin, which leads to anemia. Additional serious complications of chronic kidney disease include a condition known as chronic kidney disease mineral and bone disorder that occurs when the diseased kidneys fail to maintain proper levels of calcium and phosphorous in the blood, leading to abnormal bone hormone levels, weakened bones and vascular calcification. Bone and vascular disorders are common complications in people with chronic kidney disease and bone disorders affect almost all patients receiving dialysis. According to the United States Renal Data System, there are over 400,000 chronic kidney disease patients receiving dialysis in the United States. Erythropoiesis stimulating agents have been approved for this indication for over twenty years. Sotatercept has the potential to differentiate itself from erythropoiesis stimulating agents in this patient population because of its positive effects on bone metabolism observed following the administration of sotatercept in preclinical models, healthy volunteers and cancer patients. Additionally, in mouse models of vascular calcification, sotatercept caused a reduction of calcified deposits in the aorta.

Sotatercept Clinical and Preclinical Development

Sotatercept is a soluble receptor fusion protein consisting of the extracellular domain of the activin receptor type IIA (ActRIIA) linked to the Fc domain of human IgG1. Sotatercept acts as a protein trap for TGF-β superfamily ligands that signal through the ActRIIA receptor. Sotatercept has increased red blood cells in multiple clinical trials.

Ongoing Phase 2 Clinical Trials of Sotatercept

Our collaboration partner, Celgene, is currently conducting four Phase 2 clinical trials of sotatercept in patients with β-thalassemia, MDS and chronic kidney disease. The FDA has granted orphan designation for sotatercept for the treatment of β-thalassemia. We understand that Celgene plans to submit an application for orphan drug designation of sotatercept for treatment of MDS. Through collaborations with leading academic institutions, Celgene is also overseeing three investigator-sponsored trials.

Celgene-Sponsored Clinical Trials

β-thalassemia. Celgene is conducting a Phase 2 clinical trial of sotatercept designed as an ascending dose study to determine the safety and efficacy of sotatercept in adults with β-thalassemia. The dose levels to be studied are 0.1, 0.3, 0.5 mg/kg and 0.75 mg, with the possibility of further dose

Table of Contents

escalation up to 1.0 and 1.5 mg/kg, given subcutaneously once every three weeks for a period of 6 cycles with continued treatment at the discretion of the investigator for up to 22 months. Each cohort includes six or more patients during the dose escalation phase, followed by an expansion phase at a selected dose level in up to ten additional patients. The first patient in the trial was first dosed in November 2012. Celgene has completed enrolling the 0.1, 0.3, and 0.5 mg/kg cohorts and is now enrolling patients in the 0.75 mg/kg cohort. The primary outcome measure of the trial is to identify a safe dose level and to measure efficacy (1) in transfusion dependent patients by a reduction of transfusion burden by ≥ 20% compared to the pretreatment transfusion burden for each patient and (2) in non-transfusion dependent patients by an increase in hemoglobin level by ≥1 g/dL compared to the baseline hemoglobin, sustained for 12 weeks. This trial will also evaluate as exploratory endpoints the effects of sotatercept on iron overload, which is an important cause of morbidity and mortality associated with β-thalassemia, and bone metabolism. The trial is being conducted in six sites in Italy, France, Greece, and the United Kingdom and may enroll approximately 65 patients.

Sotatercept has generated encouraging preliminary data in the ongoing Phase 2 clinical trial of sotatercept in β-thalassemia patients.

As shown in the figure below, sotatercept has generated encouraging dose-dependent increases in hemoglobin levels in patients in the Phase 2 clinical trial who are non-transfusion dependent based on preliminary data from the three lowest dose levels in that trial.

Mean Change in Hemoglobin Level From Baseline by Dose Cohort in Non-Transfusion Dependent β-Thalassemia Patients Treated With Sotatercept

Table of Contents

Another analysis of the data from this trial also shows dose-dependent increases in hemoglobin levels. In the analysis shown below, within the first two months of receiving the first dose of sotatercept:

- 84% of non-transfusion dependent patients in each of the 0.5 and 0.3 mg/kg dose levels achieved at least a 1 g/dL increase in hemoglobin, while none of the non-transfusion dependent patients at the lowest dose level (0.1 mg/kg) achieved this threshold.

- 33%, 16% and 0% of non-transfusion dependent patients achieved a hemoglobin increase of at least 2 g/dL in the 0.5, 0.3, and 0.1 mg/kg dose levels, respectively.

Maximum Change in Hemoglobin Level From Baseline in Non-Transfusion Dependent β-Thalassemia Patients During the First 3 Cycles (Day 64) of Sotatercept Treatment

Table of Contents

The figure below shows that there is a statistically significant relationship ($p<0.001$) between drug exposure and the maximum increase in hemoglobin during the first three cycles across the three lowest dose levels of sotatercept. The x-axis shows the levels of sotatercept in patients' serum and the y-axis shows the patients' maximum change in hemoglobin. The figure illustrates that as the drug exposure in patients increases, so does the maximum increase in hemoglobin.

Relationship Between Drug Exposure and Hemoglobin Level in Non-Transfusion Dependent β-Thalassemia Patients Through the First 3 Cycles (Day 64) of Sotatercept Treatment

Only patients completing the first 3 planned treatment cycles are included.
(AUC) area under the curve; HgB, hemoglobin

We expect Celgene to establish a range of recommended sotatercept dose levels, based on these data and additional data to be gathered as the clinical trials continue. We expect that in future clinical trials, patients will begin treatment at a recommended starting dose level and to undergo individualized dose titration based on hemoglobin response and tolerability to achieve and maintain an appropriate hemoglobin level. We expect Celgene to continue to dose escalate in this trial with the objective to determine the dose range for evaluation in the expansion stage of this trial. If this activity is confirmed with an acceptable safety profile, we and Celgene plan to initiate pivotal trial(s) in β-thalassemia by the end of 2014 or early 2015. At the dose levels that have been studied to date, we have not yet observed an effect in the transfusion dependent patients. Based on currently projected timelines, which are subject to change, we expect additional data from this clinical trial to become available as follows: data from additional dose levels and extended treatment in patients from the dose escalation portion of the clinical trial in the second quarter of 2014, and additional data in the fourth quarter of 2014.

MDS. Celgene is conducting a Phase 2 clinical trial of sotatercept for the treatment of anemia in patients with low-or intermediate-1 risk MDS. The dose levels to be studied are 0.1, 0.3, 0.5 and 1.0 and up to 2.0 mg/kg given subcutaneously once every three weeks for five cycles, and up to three additional cycles for late responders, with continued treatment at the discretion of the investigator. Each cohort may include up to 20 patients receiving a single dose level during the dose escalation

Table of Contents

phase, followed by an expansion phase at a selected dose level in up to 15 additional patients. The first patient in the trial was first dosed in December 2012. Celgene has currently completed the 0.1, 0.3 and 0.5 mg/kg cohorts and is now enrolling patients in the 1.0 mg/kg cohort. Dose escalation may go up to 2.0 mg/kg. The primary outcome measure is erythroid hematological improvement (HI-E). For patients who require transfusions of <4 units of red blood cells in the eight weeks prior to dosing, HI-E is an increase in hemoglobin of ≥1.5 g/dL sustained over a period ≥8 weeks in the absence of red blood cell transfusions. For subjects that require transfusions of ≥4 units of red blood cells in the eight weeks prior to dosing, HI-E is a decrease of ≥4 units of red blood cells transfused over a period of eight weeks compared to the number of units transfused in the eight weeks prior to treatment. This trial will also evaluate the effects of sotatercept on iron overload and bone metabolism. The trial is being conducted at up to 23 sites in the United States and France and may enroll up to 115 patients. Based on currently projected timelines, which are subject to change, we expect additional data from this clinical trial to become available as follows: data from the dose escalation portion of the clinical trial in the second quarter of 2014, and additional data in the fourth quarter of 2014.

Chronic Kidney Disease. Celgene is conducting two Phase 2 clinical trials with sotatercept in patients with chronic kidney disease. The first is a Phase 2 clinical trial with sotatercept designed as a randomized, placebo-controlled dose escalation study to evaluate the pharmacokinetics, safety, efficacy, tolerability and pharmacodynamics of sotatercept for the correction of anemia in patients with chronic kidney disease on hemodialysis. The first patient in the trial was first dosed in August 2010. The first dose level was 0.1 mg/kg administered subcutaneously as a single dose. Subsequent dose levels to be studied are 0.3, 0.5 and 0.7 mg/kg administered subcutaneously once every four weeks for up to eight cycles. Each cohort will include up to 12 (nine sotatercept-treated and three placebo-treated) patients receiving a single dose level during the dose escalation phase, followed by an additional cohort at a selected dose level. Celgene has completed enrollment in the 0.1, 0.3 and 0.5 mg/kg cohorts and is now enrolling patients in the 0.7 mg/kg cohort. The primary endpoints are pharmacokinetics and safety. Other endpoints include effects on hemoglobin and serum markers of bone metabolism. The trial is being conducted at up to 21 sites in the United States and may enroll up to 56 patients.

Early data from this trial are encouraging. An interim analysis from this clinical trial indicates that sotatercept produces dose dependent increases in hemoglobin in end stage renal disease patients on hemodialysis. The data will be presented at the National Kidney Foundation Spring Clinical Meeting in April 2014.

Based in part on these interim data, and previously observed effects of sotatercept on bone biomarkers, Celgene has initiated a second phase 2 clinical trial in Europe with sotatercept in patients with end stage renal disease (ESRD) who are on hemodialysis. The first patient in this trial was first dosed in December 2013. The study is designed as a two-part study to assess the safety and efficacy of sotatercept as a therapy to treat anemia and to control the adverse manifestations of chronic kidney disease-mineral and bone disorder (CKD-MBD). Patients in both parts of the study must first be on a stable dose of an erythropoiesis stimulating agent (ESA) to maintain hemoglobin levels and, after an ESA treatment free period of approximately five days, will then be switched to treatment with sotatercept.

The first part is a dose-escalation study of intravenous and subcutaneous routes of administration of sotatercept in approximately 60 patients to evaluate pharmacokinetics, safety and tolerability. Patients in the dose escalation part of the study will be given sotatercept once every two weeks up to a total of eight doses and followed for approximately four months after their last dose. The first part of the study is designed to inform the dosing regimens to be tested in the second part of the clinical trial. The second part will be a randomized, controlled study of approximately 230 patients to evaluate the efficacy and safety of sotatercept versus an erythropoiesis stimulating agent. Efficacy measures for part two of the study include the change in mean hemoglobin concentration from baseline and the ability of sotatercept to maintain patients' hemoglobin levels within a target range after switching from an ESA

Table of Contents

to sotatercept. Measures of biomarkers for bone formation and bone resorption and for mineral metabolism also will be studied, along with imaging of vascular calcification.

Sotatercept Investigator Sponsored Trials

Through collaborations with leading academic institutions, Celgene is overseeing investigator-sponsored trials in multiple myeloma, Diamond-Blackfan anemia and myelofibrosis.

Multiple myeloma is a cancer of the bone marrow that leads to the uncontrolled growth of certain white blood cells, causing bone marrow failure, bone pain, bone fractures and kidney problems. Nearly all multiple myeloma patients suffer from anemia. Investigators at the Massachusetts General Hospital are conducting a trial to explore the possibility that the combination of anti-myeloma therapies Revlimid® and dexamethasone together with sotatercept may reduce the growth of cancer cells along with improving anemia as well as bone lesions that often occur in patients with multiple myeloma.

Diamond-Blackfan anemia is a rare and severe anemia that is present at birth in affected individuals. Investigators at North Shore Long Island Jewish Health System are conducting a trial to determine the safety and efficacy of sotatercept in adults with Diamond-Blackfan anemia who are red blood cell transfusion-dependent.

Myelofibrosis is an acquired disease of the bone marrow that results in replacement of the bone marrow with fibrotic tissue leading to bone marrow failure and inability to make new blood cells, including red blood cells, which leads to anemia. Investigators at the MD Anderson Cancer Center are conducting a trial to determine the safety and efficacy of sotatercept in patients with myeloproliferative neoplasm-associated myelofibrosis and anemia.

Completed Clinical Trials

Six human clinical trials of sotatercept, including Phase 1 clinical trials in healthy volunteers and Phase 2 clinical trials of patients with multiple myeloma, breast cancer, and non-small cell lung cancer, collectively involving over 160 patients have been conducted to date. In healthy volunteers, we observed increases in red blood cells and hemoglobin. The mean change in hemoglobin for the patients who received a single dose of 1.0 mg/kg was almost 3 g/dL, which is similar to receiving a transfusion of three units of blood. We have also shown that in a randomized, placebo-controlled trial in patients with multiple myeloma receiving melphalan, prednisolone and thalidomide, sotatercept produced dose-dependent increases in hemoglobin. In the placebo and 0.1 mg/kg sotatercept cohorts, none of the patients achieved at least a 1.5 g/dL increase in hemoglobin at day 29 of the trial compared to their baseline levels. In the 0.3 and 0.5 mg/kg sotatercept cohorts, 13% and 38% of the patients, respectively, achieved at least a 1.5 g/dL increase in hemoglobin at day 29 of the trial compared to their baseline levels. In a randomized, placebo-controlled clinical trial in breast cancer patients who had anemia due to myelosuppressive chemotherapy, sotatercept produced dose-dependent increases in hemoglobin levels. In both the placebo and 0.1 mg/kg sotatercept cohorts, 20% of the patients had their hemoglobin levels increase to at least 11 g/dL maintained for 28 days in the absence of a red blood cell transfusion or use of an erythropoiesis stimulating agent. In the 0.3 mg/kg cohort, 22% of the patients achieved this outcome and in the 0.5 mg/kg cohort, 75% of the patients achieved this threshold. In a randomized, dose-ranging Phase 2 trial of sotatercept in patients with metastatic non-small cell lung cancer, sotatercept, administered at a fixed dose of 15 or 30 mg given subcutaneously every six weeks, produced increases in hemoglobin. In patients who did not receive red blood cell transfusions within the first four weeks, the change from baseline was at least 1 g/dL of hemoglobin for 40% of patients at week 2 and 16% of patients at week four. Given the results of these trials, we and Celgene may decide to pursue further clinical development in the future in one or more of these indications.

Table of Contents

Safety

Across the completed clinical trials, sotatercept has been generally well-tolerated. In studies with healthy volunteers, the only treatment-related serious adverse event was a report of persistent, progressive high blood pressure in one subject. While the precise cause of elevated blood pressure cannot be determined, it was an expected consequence of elevated red blood cell levels that occurred in this subject. Commonly observed adverse events included headache, infection, dizziness, hypertension, hot flush, tingling, muscle spasms, limb injury, fatigue and asthenia. In three studies of patients with cancer (myeloma, breast and lung cancer), one sudden death was reported in a myeloma patient. The event was evaluated as probably related to the concurrent anti-myeloma therapy of melphalan, prednisolone and thalidomide and possibly related to sotatercept. One patient with advanced breast cancer experienced serious adverse events of perforated gastric ulcer and peptic ulcer disease that were evaluated as possibly related to sotatercept. One patient with advanced lung cancer experienced a serious adverse event of a cerebrovascular accident (blockage of a blood vessel in the brain) that was suspected as related to treatment.

Among the ongoing clinical trials managed by Celgene, as of December 23, 2013, no treatment-related serious adverse events have been reported in the MDS trial. In the β-thalassemia trial as of December 9, 2013, three patients have exhibited serious adverse events that were suspected as related to sotatercept: bone pain, superficial thrombophlebitis (an inflamed blood clot in a superficial vein) and ventricular extrasystoles (ventricular heart contractions). One patient at the 0.5 mg/kg dose level had a treatment-related Grade 3 adverse event of ventricular extrasystoles (ventricular heart contractions) and discontinued treatment.

Sotatercept Investigational New Drug (IND) Applications

Sotatercept is the subject of three separate company-sponsored U.S. IND applications. We submitted the first IND to the FDA on March 13, 2006 for the treatment of postmenopausal osteoporosis. There are currently no studies being conducted under this IND. We submitted the second IND to the FDA on March 27, 2009 to assess the use of sotatercept for the treatment of anemia in various cancer-related indications. We transferred sponsorship of both INDs to Celgene on January 19, 2010. Under the second IND, sotatercept is currently being studied in patients with lower-risk MDS. A third IND was submitted by Celgene to the FDA on January 25, 2010 to assess sotatercept for the treatment of anemia in patients with end-stage renal disease. In addition, sotatercept is being studied in Europe under three separate Clinical Trial Applications (CTAs). The first CTA is for a Phase 2 study for the treatment of anemia in adult patients with β-thalassemia, submitted to France on December 28, 2011, to the United Kingdom on July 26, 2012, to Italy on July 27, 2012, and to Greece on November 23, 2012. The second CTA is for a Phase 2 study for the treatment of anemia in patients with lower-risk MDS, submitted to France on October 10, 2012. The third CTA is for a Phase 2 study for the treatment of anemia in patients with chronic kidney disease, with Belgium, Germany, Portugal, Spain, and the UK joining under the Voluntary Harmonization Procedure on June 17, 2013. Sotatercept is also being studied in the United States under three investigator-sponsored INDs.

Preclinical Studies

In preclinical studies, RAP-011 (the mouse equivalent of sotatercept) was evaluated in a broad range of animal pharmacology studies to assess its biological effects. RAP-011 has been shown to increase red blood cell counts in mice, rats, and monkeys. RAP-011 showed increased hemoglobin and red blood cell counts in mouse models of β-thalassemia and MDS, demonstrating decreased ineffective erythropoiesis in these models. RAP-011 was also able to prevent chemotherapy-induced anemia in a mouse model of this condition and was able to correct anemia in a mouse model of chronic kidney disease. RAP-011 increased bone mineral density in ovariectomized mice and has demonstrated positive effects in mice on bone lesions and bone metastases in a number of cancer models including models of

Table of Contents

multiple myeloma. The preclinical activity of sotatercept is also being evaluated in a mouse model of sickle cell disease.

ACE-536 Clinical and Preclinical Development

ACE-536 is a soluble receptor fusion protein consisting of a modified extracellular domain of the activin receptor type IIB (ActRIIB) linked to the Fc domain of human IgG1.

Ongoing Phase 2 Clinical Trials of ACE-536

We are conducting Phase 2 clinical trials of ACE-536 in patients with β-thalassemia and in patients with MDS. The FDA has granted orphan designation for ACE-536 for the treatment of β-thalassemia and for the treatment of MDS.

β-thalassemia. We are conducting a Phase 2 clinical trial of ACE-536, designed as an ascending dose trial to evaluate the safety and efficacy in patients with β-thalassemia. The dose levels to be studied are 0.2, 0.4, 0.6, 0.8 and 1.0 mg/kg given subcutaneously once every three weeks for up to 85 days. Each cohort will include three to six patients receiving a single dose level during the dose escalation phase. This will be followed by an expansion phase at a selected dose level in up to 20 patients. We are in the process of amending the protocol to include additional types of transfusion-dependent patients, to increase the size of the expansion cohort of the trial and to potentially study higher dose levels of ACE-536. The first patient in the trial was first dosed in March 2013. We have completed enrollment of the 0.2, 0.4 and 0.6 mg/kg cohorts and are currently enrolling patients in the 0.8 mg/kg cohort. The primary outcome measure is the proportion of patients who have an increase in hemoglobin of ≥1.5 g/dL from baseline for ≥14 days (in the absence of red blood cell transfusions) in non-transfusion dependent patients or a ≥20% reduction in red blood cell transfusion burden compared to the pretreatment transfusion burden in transfusion dependent patients. This trial will also examine the effects of ACE-536 on iron overload, an important cause of morbidity and mortality in β-thalassemia patients. Secondary endpoints include markers of serum iron and hemolysis. The trial is being conducted at up to seven sites in Italy and Greece, and we plan to include additional sites in Europe and may enroll up to 72 patients.

Initial data from this clinical trial is encouraging. As of January 3, 2014, preliminary data after three cycles (approximately two months) of treatment with ACE-536 show that non-transfusion dependent β-thalassemia patients in the 0.6 mg/kg dose group achieved a mean increase in hemoglobin of approximately 1.5 g/dL, while patients in the 0.2 and 0.4 mg/kg dose groups achieved a mean increase in hemoglobin of approximately 0.0 and 0.8 g/dL, respectively. Based on these data and additional data to be gathered during the clinical trial, we expect to establish a range of recommended ACE-536 dose levels. We expect that in future clinical trials, patients will begin treatment at a recommended starting dose level and to undergo individualized dose titration based on hemoglobin response and tolerability to achieve and maintain an appropriate hemoglobin level.

Based on currently projected timelines, which are subject to change, we expect data from this clinical trial to become available as follows: data from the dose escalation portion of the clinical trial during the second quarter of 2014, and additional data in the fourth quarter of 2014.

MDS. We are conducting a Phase 2 clinical trial of ACE-536 designed as an ascending dose trial in patients with low or intermediate-1 risk MDS. The dose levels to be studied are 0.125, 0.25, 0.5, 0.75, 1.0, 1.33 and 1.75 mg/kg given subcutaneously once every three weeks for up to 85 days. Each cohort will include three to six patients receiving a single dose level during the dose escalation phase. This will be followed by an expansion phase at a selected dose level in up to 30 patients. The first patient in the trial was first dosed in January 2013. We have currently completed enrollment in the 0.125, 0.25, 0.5, 0.75 and 1.0 mg/kg cohorts and are now enrolling patients in the 1.33 mg/kg cohort. The primary outcome measure is the proportion of patients who have an increase of hemoglobin ≥ 1.5 g/dL from

Table of Contents

baseline for 14 days in the absence of red blood cell transfusions in non-transfusion dependent patients or a ≥50% or ≥4 unit reduction of red blood cell transfusions over a period of eight weeks compared to pretreatment transfusion burden in transfusion-dependent patients. This trial will also examine the effects of ACE-536 on iron overload. The trial is being conducted at up to nine sites in Germany and may enroll up to 72 patients. Based on currently projected timelines, which are subject to change, we expect additional data from this clinical trial to become available as follows: data from the dose escalation portion of the clinical trial during the second quarter of 2014, and additional data in the fourth quarter of 2014.

Completed Phase 1 Clinical Trial

ACE-536 was studied in a double-blind, placebo-controlled, randomized, ascending dose Phase 1 clinical trial in 32 healthy volunteers. ACE-536 produced dose-dependent increases in hemoglobin and red blood cells. The proportion of subjects with a hemoglobin increase of ≥1.0 g/dL increased on a dose-dependent basis, with approximately 80% of subjects in the 0.25 mg/kg dose level achieving this threshold.

Safety

In the completed Phase 1 clinical trial in healthy volunteers, ACE-536 was well-tolerated. No ACE-536 related serious adverse events were reported in the completed Phase 1 clinical trial. Commonly observed possibly or probably treatment-related adverse events included injection site bruising, injection site blemish, dry skin, numbness, muscle spasms, muscle pain, generalized itchiness and raised rash. In the ongoing Phase 2 clinical trials, there have been no ACE-536 related serious adverse events reported as of January 3, 2014. One patient in the ACE-536 thalassemia trial who was treated at the 0.8 mg/kg dose level had dose-limiting toxicity of worsening lumbar spine bone pain. The patient had a dose reduction to 0.6 mg/kg for the second cycle and subsequently withdrew from the study.

ACE-536 Investigational New Drug (IND) Applications

ACE-536 is being studied in the United States under an IND that we submitted to the FDA on June 14, 2011. The indication identified in the IND is for the treatment of anemia in patients with MDS. No studies are being conducted under this IND at this time. In addition, ACE-536 is being studied in Europe under two separate Clinical Trial Applications (CTAs). The first is for a Phase 2 study for the treatment of anemia in adult patients with β-thalassemia, submitted to Italy on August 29, 2012, to Turkey on June 14, 2013, and to Greece on July 2, 2013. The second is for a Phase 2 study for the treatment of anemia in patients with low- or intermediate-1 risk MDS, submitted to Germany on August 21, 2012.

Preclinical Studies

A number of preclinical pharmacology studies have been conducted with ACE-536 or its mouse version, RAP-536, that demonstrate its effects on red blood cells, hemoglobin and hematocrit. Collectively ACE-536 and RAP-536 have shown activity in mouse models of β-thalassemia, MDS, chemotherapy-induced anemia, acute blood loss and renal anemia.

β-thalassemia. RAP-536 has been evaluated in a series of studies using a mouse model of β-thalassemia. These mice carry deletion mutations in the β-globin genes, resulting in a deficiency of β-globin protein and hematologic abnormalities very similar to those seen in human β-thalassemia patients, including severe anemia and the formation of hemichromes resulting in ineffective erythropoiesis. These mice also exhibit severe complications common in patients with thalassemia, such as an enlarged spleen, bone loss and iron overload. In these mice, RAP-536 treatment improved

Table of Contents

numerous hematologic parameters, including significant increases in red blood cell count, hemoglobin levels, and hematocrit, decreased serum erythropoietin, normalized red blood cell size, and reduced red blood cell breakdown, as measured by serum bilirubin.

Representative blood smears were taken from the β-thalassemia mouse studies for both the placebo-treated animals and the RAP-536 treated animals. As shown in the image below, RAP-536 improved red blood cell morphology by reducing the number of poorly formed and damaged red blood cells, and reducing the amount of cellular debris that results from dying red blood cells.

Importantly, RAP-536 improved the maturation of later stage red blood cell precursor populations, in the bone marrow and spleen, with concomitant reductions in the earlier-stage red blood cell precursor populations. We believe RAP-536 reduced the ineffective erythropoiesis by decreasing the formation of harmful hemichromes. It appears that RAP-536 may achieve this effect in part by stimulating the proteasome, thus promoting the removal of unpaired α-hemoglobin and stimulating red blood cell maturation.

This reduction in ineffective erythropoiesis reduced severe and common complications of the disease in mice, evidenced by reduced iron deposition in organs, reduced spleen weights and normalized bone density. Based on the numerous beneficial effects of RAP-536 in this mouse model of β-thalassemia, we believe that it is modifying the disease and has the potential to do so in human patients.

MDS. In a mouse model of MDS, RAP-536 treated animals had statistically significant increases in red blood cell count, hemoglobin levels and hematocrit compared to controls. Additionally, RAP-536 reduced the ineffective erythropoiesis as evidenced by the improvement in the ratio of red blood cell precursors to other cells in the bone marrow.

Sickle Cell Disease. We and Celgene are exploring the preclinical activity of ACE-536 in a mouse model of sickle cell disease.

Taken together, our clinical and preclinical results suggest that ACE-536 could be a meaningful novel therapy to treat anemia.

Table of Contents

Dalantercept

Inhibiting Angiogenesis to Limit Tumor Growth

Angiogenesis is a process by which new blood vessels are formed. Angiogenesis can be simplified to two major stages the proliferative stage followed by the maturation stage. During the proliferative stage, vascular endothelial cells, the cells lining the inside of the blood vessels, multiply in number and migrate to the site where a new vessel will be formed. This proliferative stage is followed by the maturation stage during which the endothelial cells coalesce to form tubes which are then stabilized through the recruitment of perivascular cells that form an outer layer of the blood vessels resulting in fully formed, functional vessels.

Tumors depend on angiogenesis to form new blood vessels to supply nutrients and oxygen to feed the rapidly growing malignant cells. The principal molecule driving the proliferative stage of angiogenesis in tumors is a protein called vascular endothelial growth factor (VEGF). Inhibiting VEGF-driven angiogenesis to control tumor growth has become an important and widely-used approach to cancer treatment. There are several FDA-approved cancer drugs that inhibit the VEGF pathway, with over $8 billion in aggregate worldwide sales. Despite the success of these drugs, many patients fail to respond or develop resistance to VEGF pathway inhibitor therapy, resulting in an unmet need for new therapies to inhibit angiogenesis by a different mechanism.

We are using our knowledge of the TGF-β superfamily to develop dalantercept, a novel protein therapeutic candidate targeting the maturation stage of angiogenesis. Recently, the activin receptor-like kinase 1 (ALK1) has been recognized as a key regulator of the maturation stage of angiogenesis. ALK1 is one of the 12 receptors for ligands in the TGF-β superfamily and is found primarily on endothelial cells. The importance of the ALK1 pathway in angiogenesis was discovered, in part, through research into the genetic basis of the disease hereditary hemorrhagic telangiectasia 2 (HHT-2) in which patients manifest vascular defects including reduced ability to form capillary beds, which are the networks of small blood vessels that connect arteries to veins and are necessary for nutrient and waste exchange in tissues. This research revealed that these patients have only one of two functional copies of the ALK1 gene.

We reasoned that leveraging the biology of the ALK1 pathway to inhibit maturation of blood vessels could impair the growth of tumors by limiting the development of capillary beds within the tumor. To test this hypothesis, mice with a predisposition to develop tumors were bred to have only one, rather than two copies, of the ALK1 gene. In response to the loss of half of the ALK1 genes, tumor growth and size and blood vessel density in the tumor were reduced by half. These results and additional research in the field have established the ALK1 signaling pathway as a promising target for developing a new class of anti-angiogenesis agents ALK1 pathway inhibitors.

We believe one promising opportunity for dalantercept will be its use in combination with VEGF pathway inhibitors because these agents target distinct sequential steps in angiogenesis. Moreover, we and others have hypothesized that agents, such as dalantercept, that inhibit vessel maturation are able to sensitize the tumor vasculature to the anticancer effects of VEGF pathway inhibition. We believe that newly formed blood vessels become more resistant to VEGF pathway inhibitors as they mature. Therefore we believe that by preventing blood vessel maturation, dalantercept may maintain newly formed vessels in an immature state that increases their susceptibility to VEGF pathway inhibitors.

We and our academic collaborators have also shown in two mouse cancer models that treatment with dalantercept decreases metastases. This is in contrast to VEGF pathway inhibitors that increase metastases in mouse cancer models.

We believe that a combination of ALK1 and VEGF pathway inhibitors could have application in a number of different oncology indications where VEGF pathway inhibitors are currently used. The currently approved VEGF pathway inhibitors include Avastin® (bevacizumab), Nexavar® (sorafenib),

Table of Contents

Sutent® (sunitinib), Inlyta® (axitinib), and Votrient® (pazopanib). Four large markets for which these drugs have been approved are non-small cell lung cancer, colorectal cancer, renal cell carcinoma and liver cancer.

Non-Small Cell Lung Cancer (NSCLC). The National Cancer Institute estimates there will be 228,190 new cases of lung cancer in the United States in 2013 with 159,480 deaths. In 2012, sales of Avastin® in NSCLC were $1.2 billion in the United States and $1.7 billion worldwide.

Colorectal Cancer. The National Cancer Institute estimates there will be 142,820 new cases of colon cancer or rectal cancer in the United States in 2013 with 50,830 deaths. In 2012, sales of Avastin® for colorectal cancer were $1.2 billion in the United States and $3.6 billion worldwide.

Renal Cell Carcinoma. The National Cancer Institute estimates there will be 65,150 new cases of renal cell carcinoma in the United States in 2013 with 13,680 deaths. In 2012, U.S. sales of drugs for renal cell carcinoma were $1.2 billion, of which $800 million were anti-angiogenesis drugs that target the VEGF pathway, principally Sutent®, Nexavar® and Avastin®. Worldwide sales in 2012 of drugs for renal cell carcinoma were $3.1 billion, of which $2.3 billion were drugs that target the VEGF pathway.

Liver Cancer. The National Cancer Institute estimates there will be 30,640 new cases of liver cancer in the United States in 2013 with 21,670 deaths. The only drug approved in the United States for the treatment of liver cancer is the VEGF pathway inhibitor Nexavar®. In 2012, sales of Nexavar® for liver cancer were $189 million in the United States and $756 million worldwide.

Other Tumors. One or more anti-angiogenesis agents are also approved as treatments for neuroendocrine tumors, thyroid cancer and glioblastoma.

Developing Indications. It is believed that angiogenesis is important in the growth and spread of a number of additional highly-vascularized cancers, including endometrial cancer (cancer of the uterus), ovarian cancer, and head and neck cancer. While no anti-angiogenesis agents are approved in the U.S. for these indications, Avastin® is approved in Europe for the treatment of ovarian cancer.

The first two cancers for which we are studying the combination of dalantercept plus a VEGF pathway inhibitor are renal cell carcinoma and liver cancer. In renal cell cancer, sunitinib and axitinib are the most prescribed VEGF pathway inhibitors for first and second line patients, respectively. In the first line setting, sunitinib results in progression-free survival rates of approximately 11 months. In the second line setting, for patients whose disease had progressed despite receiving sunitinib in the first line setting, axitinib produced a progression-free survival rate of approximately 4.8 months. We believe the combination of dalantercept plus axitinib in the second line setting has the potential to increase the rate of progression-free survival greater than axitinib alone. In liver cancer, the VEGF pathway inhibitor, sorafenib, is approved in the first line setting yet the unmet medical need remains significant. In the first line setting, sorafenib results in time to progression of approximately 5.5 months.

Dalantercept Clinical and Preclinical Development

Dalantercept is comprised of the extracellular domain of the ALK1 receptor linked to the Fc domain of IgG1. Dalantercept acts as a ligand trap for ligands in the TGF-β superfamily that signal through the ALK1 receptor. We have completed a Phase 1 trial of dalantercept and are pursuing a program of ongoing and planned Phase 2 trials seeking to demonstrate single agent activity of dalantercept for advanced solid tumors and activity of dalantercept in combination with approved VEGF pathway inhibitors or chemotherapy in advanced solid tumors.

Table of Contents

Ongoing and Planned Phase 2 Clinical Trials of Dalantercept

We are currently conducting two Phase 2 clinical trials of dalantercept in head and neck cancer and renal cell carcinoma. Additionally, through collaborations with a National Cancer Institute funded collaborative research group, the Gynecologic Oncology Group, we are overseeing an additional Phase 2 clinical trial in ovarian cancer. We plan to initiate a trial of dalantercept in hepatocellular carcinoma in the first half of 2014. We plan to submit applications for orphan designation of dalantercept for those indications or subsets of indications that meet FDA requirements for orphan status.

Acceleron Sponsored Clinical Trials

Squamous Cell Carcinoma of the Head and Neck. We are conducting a single agent Phase 2 clinical trial of dalantercept in an ascending dose trial in patients with recurrent or metastatic squamous cell carcinoma of the head and neck. The first patient in the trial was first dosed in October 2011. After an initial cohort of two patients treated at a fixed dose level of 80 mg, we amended the trial and began recruitment of patients under the amended protocol in the first quarter of 2012 to study the dose level of 0.6 mg/kg given subcutaneously once every three weeks. The protocol was subsequently amended to increase the dose level of dalantercept to 1.2 mg/kg. Patients continue to receive dalantercept until there is disease progression (either clinically or as measured by analysis of radiographic imaging according to RECIST criteria) or dalantercept is no longer tolerated. The primary outcome measure is objective response rate as measured by RECIST criteria, and there are a number of secondary outcome measures of tumor response. The trial is being conducted in 12 centers in the United States, and we completed enrollment in July 2013 with a total of 46 patients, including two patients treated at the 80 mg dose, 13 at the 0.6 mg/kg dose, and 31 at the 1.2 mg/kg dose. Of these 46 patients, 41 patients (one patient at 80 mg, 13 patients at 0.6 mg/kg, and 27 patients at 1.2 mg/kg) were evaluable for radiological response according to RECIST criteria as of December 20, 2013. The preliminary data for these 41 patients are as follows: no patients at 80 mg, three patients (23%) at 0.6 mg/kg and ten patients (37%) at 1.2 mg/kg achieved stable disease as their best response at the beginning of their third cycle and, at the 1.2 mg/kg dose level, one patient (2.4%) achieved a partial response. None of these patients achieved a complete response. These preliminary data suggest dalantercept has dose dependent but modest single agent activity in patients with advanced squamous cell carcinoma of the head and neck. We believe the greatest potential for dalantercept will be in combination with VEGF pathway inhibitors or in combination with cytotoxic chemotherapy.

Renal Cell Carcinoma. We are conducting a two-part Phase 2 clinical trial of dalantercept in combination with axitinib, an approved VEGF pathway inhibitor, in patients with advanced renal cell carcinoma. Part one of this trial is designed as a single-arm dose escalation and expansion stage with the primary endpoint of evaluating the safety and tolerability of various dose levels of dalantercept in combination with axitinib to select a dose level of dalantercept (in combination with axitinib) for further study if merited. The dose levels of dalantercept studied in the dose escalation stage were 0.6, 0.9, and 1.2 mg/kg given subcutaneously once every three weeks. The number of patients enrolled at the 0.6, 0.9 and 1.2 mg/kg dose levels were four, four and five patients, respectively. The dose level of 1.2 mg/kg was selected for use in the expansion phase and we are now enrolling up to 20 additional patients in this stage of the study. The first patient in the trial was first dosed in January 2013. Patients continue to receive dalantercept and axitinib until there is disease progression (either clinically or as measured by RECIST criteria) or the combination is no longer tolerated. Up to a total of 44 patients may be enrolled in the dose escalation and expansion part of the trial. Part two of the trial will be a randomized comparison of the selected dose of dalantercept in combination with axitinib versus axitinib alone with a total of 112 patients. The primary endpoint of part two of the trial will be progression-free survival. The trial is currently being conducted in 7 sites in the United States.

Table of Contents

We believe that early preliminary data from this trial are encouraging. No dose-limiting toxicities have been observed during the 29 day assessment period for each dose cohort. Of the 13 patients enrolled in the dose escalation part of the trial, seven (54%) had received one prior therapy and six (46%) had received ≥ 2 prior therapies, including two patients with ≥ 2 prior VEGF-pathway inhibitors. As of December 24, 2013, six of eleven (55%) evaluable patients completed ≥ 6 cycles (approximately 4.5 months) of treatment, including two of four patients at the 0.6 mg/kg dose level, two of four patients at the 0.9 mg/kg dose level and two of three patients at the 1.2 mg/kg dose level. These data provide preliminary evidence that dalantercept can be safely combined with the VEGF-pathway inhibitor axitinib in patients with renal cell carcinoma. As of the most recent analysis (August 28, 2013) of tumor response according to RECIST criteria in the first two cohorts, one patient had achieved a partial response and one patient had achieved stable disease at the 0.6 mg/kg dose level, and one patient had achieved a partial response and three patients had achieved stable disease at the 0.9 mg/kg dose level. Data from patients at the 1.2 mg/kg dose level have not yet been analyzed.

As of the most recent analysis of tumor response according to RECIST criteria (August 28, 2013), one patient had achieved a partial response and one patient had achieved stable disease at the 0.6 mg/kg dose level and one patient had achieved a partial response and three patients had achieved stable disease at the 0.9 mg/kg dose level. Data from patients at the 1.2 mg/kg level have not been analyzed.

Based on currently projected timelines, which are subject to change, we expect to initiate part two of this trial by the end of the first quarter or the beginning of the second quarter of 2014, which, if successful, we expect would enable a Phase 3 trial. We expect additional dose escalation data to be available when we initiate part two of the trial.

Hepatocellular Carcinoma

In the first half of 2014, we plan to initiate a Phase 2 single-arm dose escalation and expansion clinical trial of dalantercept in combination with sorafenib, an approved VEGF pathway inhibitor, in patients with hepatocellular carcinoma. The primary endpoint will be to evaluate the safety and tolerability of various dose levels of dalantercept in combination with sorafenib. Secondary endpoints are expected to include time to progression, progression-free survival, disease control rate, and overall survival. The dose levels planned are 0.9 mg/kg of dalantercept given subcutaneously once every three weeks in combination with 400 mg sorafenib given once daily, 1.2 mg/kg of dalantercept given subcutaneously once every three weeks in combination with 400 mg sorafenib given once daily, and 1.2 mg/kg of dalantercept given subcutaneously once every three weeks in combination with 400 mg sorafenib given twice daily. Each cohort will include up to six patients receiving a single dose level during the dose escalation phase, followed by an expansion phase in up to 20 additional patients. Patients will continue to receive dalantercept and sorafenib until there is disease progression (either clinically or as measured by RECIST criteria) or the combination is no longer tolerated.

Gynecologic Oncology Group (GOG) Sponsored Trials

The Gynecologic Oncology Group, one of the National Cancer Institute's funded collaborative cancer research groups, sponsored two Phase 2 clinical trials to study the activity of dalantercept at a dose level of 1.2 mg/kg given as a single agent via subcutaneous injection every three weeks. The first trial was in patients with recurrent or persistent endometrial cancer and the second trial is in patients with recurrent or persistent ovarian cancer. Both of these clinical trials were designed as two part studies to assess the activity of dalantercept based on either of two endpoints: RECIST-defined response rate or progression free survival at 6 months. If there is sufficient activity in the first part of the trial, additional patients will be enrolled in the second, expanded part of the trial. The endometrial cancer study enrolled 28 patients in part one. Of the 28 patients, 16 (57.1%) achieved stable disease and 5 (17.9%) were alive and progression free for at least 6 months. Of these 5 patients, 3 were alive

Table of Contents

and progression free without receiving non-protocol therapy for at least 6 months. Fatigue, anemia, constipation, and edema were the most commonly reported toxicities regardless of attribution. The GOG has notified us that there was not sufficient activity to enroll additional patients in the second part of the endometrial cancer trial. The GOG ovarian cancer study enrolled 30 patients to part 1. We anticipate that in the middle of 2014, we may receive notification from the GOG if there is sufficient activity to enroll additional patients in the second part of the ovarian cancer trial.

Phase 1 Trial Results

A Phase 1 ascending dose trial evaluated the safety, tolerability, pharmacokinetics and anti-tumor activity of dalantercept in patients with advanced solid tumors. Dalantercept was given subcutaneously approximately once every three weeks until disease progression. Thirty-seven patients were enrolled in dose groups at 0.1, 0.2, 0.4, 0.8, 1.6, 3.2 and 4.8 mg/kg. In this trial, dalantercept demonstrated anti-tumor activity based on decreases or stabilization of tumor size. As shown in the figure below, out of the 29 evaluable patients treated, one (3%) had a partial response and 13 (45%) had stable disease according to RECIST criteria. Of the 13 who experienced stable disease, eight experienced stable disease for at least three months. Treatment continued until the patient experienced progressive disease.

The figure below displays each patient's best overall response by the maximum percent change decrease in target lesion size. The dose level each patient received is shown below their bar.

Best Overall Response by the Maximum Percent Change Decrease in Target Lesion Size According to RECIST v1.1 Criteria

In addition to these effects on tumor size, dalantercept demonstrated likely anti-angiogenic activity evidenced by a reduction of tumor metabolic activity as well as decreases in tumor blood flow. Lastly, some patients were observed to have dilated blood vessels in the skin, similar to those in HHT-2 patients, suggesting ALK1 pathway inhibition.

Table of Contents

Safety

In clinical trials to date, dalantercept has been generally well-tolerated. In the initial Phase 1 clinical trial in advanced cancer patients, five patients out of 37 experienced serious adverse events deemed treatment-related that were reported as left ventricular dysfunction, fatigue, fluid overload, and congestive heart failure. Two of these patients had prior coronary artery disease. In subsequent trials fluid overload has been successfully managed with diuretics. As of December 24, 2013, the following treatment related adverse events have been observed in our ongoing clinical trials. Two patients in the head and neck cancer clinical trial have experienced serious adverse events of fluid accumulation around the lungs that were determined to be possibly related to dalantercept. Another patient in the head and neck trial has experienced serious adverse events of tracheal obstruction and pulmonary edema that were determined to be possibly related to dalantercept. In the clinical trial of patients with endometrial cancer, seven patients have experienced treatment-related serious adverse events reported as fluid accumulation in the abdominal cavity, fluid accumulation around the lungs, rectal fistula, gastric bleeding, vomiting, anemia, and shortness of breath. In the clinical trial of patients with ovarian cancer, one patient has experienced treatment related serious adverse events reported as hypokalemia (decreased potassium), anorexia, dehydration and increased creatinine. In the renal cell carcinoma trial, there have been no dalantercept-related serious adverse events. Adverse events associated with axitinib did not occur with higher than expected frequency or severity.

Dalantercept Investigational New Drug (IND) Applications

Dalantercept is being studied in the United States under an IND that we submitted to the FDA on July 29, 2009 for the treatment of patients with advanced solid tumors or multiple myeloma. Dalantercept is also being studied in the United States under two INDs sponsored by the Gynecologic Oncology Group: the first was submitted on August 2, 2012 for the treatment of recurrent/persistent endometrial carcinoma and the second submitted on September 25, 2012 for the treatment of recurrent/persistent ovarian carcinoma.

Preclinical Studies

We have demonstrated that dalantercept as a single agent inhibits tumor growth and angiogenesis in a variety of mouse models of cancer. Importantly, we have shown that dalantercept is a potent inhibitor of the maturation stage of angiogenesis. This is in contrast with VEGF pathway inhibitors that target the proliferative stage of angiogenesis.

We also demonstrated that dalantercept in combination with a VEGF pathway inhibitor provides enhanced anti-tumor effects. In mice bearing human renal cell carcinoma xenografts, we and our academic collaborators have shown that simultaneous administration of both dalantercept and sunitinib, a VEGF-receptor tyrosine kinase inhibitor, had substantially greater efficacy than either agent alone. In another mouse model of human renal cell carcinoma that develops resistance to sunitinib, tumor

Table of Contents

growth was blocked by the simultaneous administration of dalantercept. The figures below summarize those results.

Dalantercept/Sunitinib Combination Exceeds Activity of Either Alone (Mouse Model of Renal Cell Carcinoma (A498))

Dalantercept/Sunitinib Combination Slows Tumor Growth in a Sunitinib Resistant Model (Mouse Model of Renal Cell Carcinoma (786O))

Collaboration with Drs. Wang, Bhatt, Mier, Atkins; Beth Israel Deaconess Medical Center, Boston

Development Objectives

For sotatercept and ACE-536, our development strategy, determined in collaboration with Celgene, for both β-thalassemia and MDS is to conduct similar clinical trials with each protein therapeutic candidate in each disease essentially in parallel. For each disease, we and Celgene will review the data from both studies and determine which, if either, protein therapeutic candidate to move forward into subsequent, pivotal studies. It is our goal to initiate the Phase 3 clinical trials for one or both protein therapeutic candidates in one or both of these diseases by the end of 2014 or early 2015.

In addition, we and Celgene are performing preclinical research to assess the opportunity for sotatercept and ACE-536 to treat additional red blood cell disorders known as hemoglobinopathies, which include diseases such as thalassemias and sickle cell disease. Based on our encouraging preclinical and clinical data in β-thalassemia and our emerging understanding of the mechanism of action of these protein therapeutic candidates, we believe there is a potential for activity in other diseases such as sickle cell disease and preclinical studies are currently underway.

For dalantercept, our development strategy is to continue the renal cell carcinoma trial and to initiate during 2014 part two of the trial that compares the combination of dalantercept and axitinib to axitinib alone. We plan to initiate the hepatocellular carcinoma trial in the first half of 2014. We will also work toward completion of the ongoing single agent trial in head and neck cancer. We expect to initiate during the second half of 2014, at least one additional trial of dalantercept in cancer patients in combination with an approved VEGF pathway inhibitor. We are currently considering trials of dalantercept in combination with bevacizumab in glioblastoma (a form of brain cancer), and in colorectal cancer or lung cancer in combination with chemotherapy and/or a VEGF pathway inhibitor.

Our Preclinical Pipeline

We are using our discovery platform and knowledge of the TGF-β superfamily to design and evaluate promising new protein therapeutic candidates that inhibit ligands of the TGF-β superfamily.

Table of Contents

We have preclinical stage protein therapeutic candidates in our pipeline that have shown promising activity in animal models such as:

- inhibition of liver fibrosis in mouse models of this condition;
- improvement of cardiovascular function in a mouse model of a fibrotic disorder of the lungs; and
- improvement in diseases of the eye such as in a mouse laser-induced neovascularization model of age-related macular degeneration (AMD).

ACE-083

We are developing a novel protein therapeutic candidate, ACE-083, for a first-in-human clinical trial that we expect to initiate by the end of 2014. ACE-083 acts as a trap for ligands in the TGF-β superfamily that are known to be involved in the regulation of muscle mass. By inhibiting these ligands, ACE-083 can increase muscle mass, as we have demonstrated in animal studies. ACE-083 has been designed to affect those muscles in which the drug is injected. In preclinical animal studies, ACE-083 has shown dose dependent increases in muscle mass in the injected muscles but no systemic increases in muscle mass. We are focused on the development of ACE-083 for diseases in which increases in the size and function of specific muscles may provide a clinical benefit, including inclusion body myositis, facioscapulohumeral dystrophy (FSHD) and disuse atrophy.

ACE-083 Selectively Doubles Muscle Mass in Injected Muscle with One Month of Treatment

**
p<0.05 vs. PBS (placebo) & vs. non-injected leg

Table of Contents

ALK1 Pathway Inhibitors for the Treatment of Diseases of the Eye

Although VEGF pathway inhibitors are the standard of care for age-related macular degeneration, or AMD, there is a need for improved therapies. Perivascular cell coverage may protect endothelial cells and limit the effectiveness of VEGF pathway inhibitors in AMD. By reducing the number of Perivascular cells, the activity of VEGF pathway inhibitors on unprotected endothelial cells may be potentially enhanced. Human genetic evidence indicates that patients with hereditary hemorrhagic telangiectasia (HHT-2) who lack expression of a single ALK1 gene results in defective vasculature with reduced Perivascular cell coverage. We are evaluating ALK1 pathway inhibitors, distinct from dalantercept, for use in the treatment of diseases of the eye. The combination of a VEGF pathway inhibitor and an ALK1 pathway inhibitor may lead to more effective treatment of neoangiogenesis diseases of the eye including AMD.

Our Strategic Partnerships

Collaborations with corporate partners have provided us with significant funding and access to our partners' scientific, development, regulatory and commercial capabilities. We have received more than $250.0 million from our collaborations with Celgene, Alkermes and Shire.

Celgene

On February 20, 2008 we entered into an agreement, which we refer to as the Sotatercept Agreement, with Celgene Corporation, under which we granted to Celgene worldwide rights to sotatercept. On August 2, 2011 we entered into a second agreement with Celgene for ACE-536, which we refer to as the ACE-536 Agreement under which we granted to Celgene worldwide rights to ACE-536 and also amended certain terms of the Sotatercept Agreement. These agreements provide Celgene exclusive licenses for these protein therapeutic candidates in all indications, as well as exclusive rights to obtain a license to certain future compounds.

Sotatercept Agreement. Under the terms of the Sotatercept Agreement, we and Celgene are collaborating on the development and commercialization of sotatercept. We also granted Celgene an option to license discovery stage compounds against three specified targets. Celgene paid $45.0 million and bought $5.0 million of equity upon execution of the Sotatercept Agreement and, as of September 30, 2013, we have received $34.5 million in research and development funding and milestone payments for the sotatercept program.

We retained responsibility for research, development through the end of Phase 2a clinical trials, as well as manufacturing the clinical supplies for these trials. These activities are substantially complete. Celgene is conducting the current Phase 2 trials for β-thalassemia, MDS and chronic kidney disease and will be responsible for any future clinical trials for sotatercept as well as for all future manufacture of sotatercept. We are eligible to receive future development, regulatory and commercial milestones of up to $360.0 million for the sotatercept program and up to an additional $348.0 million for each of the three discovery stage programs. None of the three discovery stage programs has advanced to the stage to achieve payment of a milestone, nor do we expect any such milestone payments in the near future.

ACE-536 Agreement. Under the terms of the ACE-536 Agreement, we and Celgene are collaborating in the development and commercialization of ACE-536. We also granted Celgene an option to license products for which Acceleron files an investigational new drug application for the treatment of anemia. Celgene paid $25.0 million to us upon execution of the ACE-536 Agreement in August 2011 and, as of September 30, 2013, we have received $28.3 million in research and development funding and milestone payments for the ACE-536 program.

Under this agreement, we retained responsibility for research, development through the end of Phase 1 and the two ongoing Phase 2 clinical trials in MDS and β-thalassemia, as well as

Table of Contents

manufacturing the clinical supplies for these studies. Celgene will conduct subsequent Phase 2 and Phase 3 clinical trials. Acceleron will manufacture ACE-536 for all Phase 1 and Phase 2 clinical trials, and Celgene will have responsibility for the manufacture of ACE-536 for Phase 3 clinical trials and commercial supplies. We are eligible to receive future development, regulatory and commercial milestones of up to $200.0 million for the ACE-536 program.

Both Agreements. Under each agreement, the conduct of the collaboration is managed by a Joint Development Committee and Joint Commercialization Committee. Other than with respect to certain matters related to our conduct of Phase 2 trials, in the event of a deadlock of a committee, the resolution of the relevant issue is determined by Celgene. Prior to January 1, 2013, Celgene paid the majority of development costs under the Sotatercept and ACE-536 Agreements. As of January 1, 2013, Celgene became responsible for paying 100% of worldwide development costs for both programs. Celgene will be responsible for all commercialization costs worldwide. We are obligated to co-promote sotatercept, ACE-536 and future products, in each case if approved, under both agreements in North America, and Celgene will pay all costs related thereto. We will receive tiered royalties in the low-to-mid 20% range on net sales of sotatercept and ACE-536. The royalty schedules for sotatercept and ACE-536 are the same. Celgene is obligated to use commercially reasonable efforts to develop and commercialize sotatercept and ACE-536. Celgene may determine that it is commercially reasonable to develop and commercialize only sotatercept or ACE-536 and discontinue the development or commercialization of the other protein therapeutic candidate, or Celgene may determine that it is not commercially reasonable to continue development of one or both of sotatercept and ACE-536. In the event of any such decision, we may be unable to progress the discontinued candidate or candidates ourselves. The agreements are terminable by either party upon a breach that is uncured and continuing or by Celgene for convenience on a country by country or product by product basis, or in its entirety. Celgene may also terminate the agreement, in its entirety or on a product by product basis, for failure of a product to meet a development or clinical trial endpoint. Termination for cause by us or termination by Celgene for convenience or failure to meet an endpoint will have the effect of terminating the applicable license, while termination for cause by Celgene will have the effect of reducing remaining royalties by a certain percentage.

Other Collaborations

Alkermes. On December 3, 2009, we entered into a Collaboration and License Agreement with Alkermes relating to a proprietary technology platform for extending the circulating half-life of certain proteins. Under the terms of the agreement, we granted Alkermes worldwide rights to apply this technology to proteins outside of the TGF-β superfamily in return for an upfront license payment. We are entitled to future development, regulatory and sales milestones and mid-single digit royalties on product sales for each drug developed and commercialized by Alkermes using this technology. To our knowledge, Alkermes is not currently developing any products using this technology.

Shire. On September 8, 2010, we entered into an agreement with Shire AG for the joint development and commercialization of ACE-031, a clinical stage protein therapeutic candidate. We granted Shire an exclusive license in markets outside of North America. Under the terms of the agreement, Shire made an upfront cash payment of $45.0 million. We received $8.7 million in research and development payments from Shire during the term of the agreement. In April 2013, we and Shire determined not to further advance the development of ACE-031, and Shire terminated our collaboration agreement, effective as of June 30, 2013 and all rights reverted to us. We currently have no plans to continue the development of ACE-031.

Competition

The development and commercialization of new drugs is highly competitive. We and our collaborators will face competition with respect to all protein therapeutics we may develop or

Table of Contents

commercialize in the future from pharmaceutical and biotechnology companies worldwide. Many of the entities developing and marketing potentially competing products have significantly greater financial resources and expertise than we do in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing. Our commercial opportunity will be reduced or eliminated if our competitors develop and commercialize products that are more effective, have fewer side effects, are more convenient or are less expensive than any products that we may develop.

If our clinical stage protein therapeutics are approved, they will compete with currently marketed drugs and therapies used for treatment of the following indications, and potentially with drug candidates currently in development for the same indications:

β-thalassemia

If either sotatercept or ACE-536 is approved for the treatment of patients with β-thalassemia, it would compete with:

Red blood cell transfusions and iron chelation therapy, such as Novartis's oral iron chelating agent, Exjade®. We are also aware that Shire is studying a new oral iron chelator in clinical trials.

Fetal hemoglobin stimulating agents, such as hydroxyurea, which are primarily used to treat patients with anemia from sickle cell disease, are sometimes used to treat patients with β-thalassemia. In addition, HQK-1001, a fetal hemoglobin stimulating agent being developed by HemaQuest Pharmaceuticals, Inc., has completed a Phase 1/2 clinical trial and an investigator sponsored Phase 2 clinical trial in patients with β-thalassemia.

Hematopoietic stem cell transplant treatment is given to a small percentage of patients with β-thalassemia, since it requires a sufficiently well-matched source of donor cells. Certain academic centers around the world are seeking to develop improvements to this approach.

Other therapies in development, including gene therapy are being developed by several different groups, including bluebird bio, Inc., Memorial Sloan Kettering Cancer Center, GlaxoSmithKline plc, and Sangamo BioSciences Inc.

MDS

If either sotatercept or ACE-536 is approved for the treatment of patients with MDS, it would compete with the following:

Recombinant erythropoietin and other erythropoiesis stimulating agents. Although these agents are not approved to treat anemia in MDS, current practice guidelines include the use of erythropoiesis stimulating agents and granulocyte colony stimulating factor agents (G-CSF) to treat patients with MDS. Additionally, Amgen's erythropoiesis stimulating agent, Aranesp®, is currently in Phase 3 clinical trials for treatment of anemia in patients with MDS.

Red blood cell transfusion and iron chelation therapy, including Exjade®, which is used to treat anemia in patients with MDS.

Immunomodulators, including Celgene's approved product, Revlimid® (lenalidomide), for the treatment of anemia of certain MDS patients.

Other therapies in development, including: an oral form of the hypomethylating agent azacitidine, known as CC-486, being developed by Celgene to treat patients with transfusion dependent anemia and thrombocytopenia due to lower risk MDS, which is currently in Phase 3

Table of Contents

clinical trials in the United States and Europe; and an anti-cancer therapy being developed by Onconova to treat patients with MDS.

Chronic Kidney Disease

If either sotatercept or ACE-536 is approved for the treatment of anemia in patients with chronic kidney disease, it would compete primarily with erythropoiesis stimulating agents that have been approved to treat these patients for over 20 years. In 2011, the Centers for Medicare and Medicaid Services (CMS) changed the reimbursement practice for erythropoiesis stimulating agents in chronic kidney disease patients on dialysis, which has led to changes in the way erythropoiesis stimulating agents are used in clinical practice, including decreasing the number of patients treated with erythropoiesis stimulating agents as well as decreasing the average dose and duration of therapy. These changes and the anticipated future introduction of biosimilar erythropoiesis stimulating agents are expected to generate additional price pressure in this market. Additionally, we are aware that Astellas Pharma and Fibrogen are developing oral, small molecule treatments that increase the production of erythropoietin to treat patients with anemia.

Oncology Therapies

We are developing dalantercept to be used in combination with VEGF pathway inhibitors for the treatment of cancer. If dalantercept is approved, it would compete with:

Other non-VEGF angiogenesis inhibitors in development, which also have the potential to be combined with VEGF pathway inhibitors or used independently of VEGF pathway inhibitors to inhibit angiogenesis. Amgen, Regeneron, MedImmune, OncoMed Pharmaceuticals, Pfizer and Tracon are each developing non-VEGF angiogenesis inhibitors.

Pfizer's fully human monoclonal antibody to the ALK1 receptor, which is in Phase 2 trials in malignant pleural mesothelioma.

In addition to the therapies mentioned above, there are many generic chemotherapy agents and other regimens commonly used to treat various types of cancer, including renal cell carcinoma, head and neck, endometrial and ovarian cancer.

Therapies for Treating Muscle Loss

We are in the process of moving our lead pre-clinical protein therapeutic candidate, ACE-083, into its initial clinical trial. We plan to develop ACE-083 for the treatment of neuromuscular disorders and other diseases characterized by a loss of muscle function. We are aware of other approaches to treating muscle loss that are in clinical trials. Novartis is developing bimagrumab (BYM338), a monoclonal antibody targeting the activin receptor type IIB (ActRIIB), in various phase 2 clinical trials to treat pathological muscle loss and weakness. Nationwide Children's Hospital, in collaboration with The Myositis Association and Parent Project Muscular Dystrophy, is conducting a phase 1 clinical trial of a gene therapy delivery of follistatin (FS344) to muscle in patients with Becker muscular dystrophy (BMD) and sporadic inclusion body myositis (sIBM). Eli Lilly is developing, LY2495655, a myostatin monoclonal antibody in phase 2 clinical trials for disuse muscle atrophy and cancer-related cachexia. Regeneron and Sanofi are developing a myostatin monoclonal antibody, REGN1033 (SAR391786), which is in phase 1 clinical development for treatment of sarcopenia. Biogen Idec is conducting a phase 1 clinical trial of BIIB023, a monoclonal antibody targeting the tumor necrosis factor (TNF)-like weak inducer of apoptosis (TWEAK), to evaluate its effects on muscle atrophy in healthy male volunteers. Atara Bio is developing PINTA 745, a myostatin inhibiting peptibody to treat protein energy wasting in patients with end stage renal disease who are on dialysis.

Table of Contents

The key competitive factors affecting the success of any approved product will be its efficacy, safety profile, price, method of administration and level of promotional activity.

Commercialization

We retain co-promotion rights with our collaboration partner, Celgene, for both sotatercept and ACE-536 in North America, and under the terms of our agreements with Celgene, our commercialization costs will be entirely funded by Celgene. We also currently retain worldwide commercialization rights for our oncology protein therapeutic candidate, dalantercept, and our muscle protein therapeutic candidate, ACE-083. We intend to build hematology, oncology and neuromuscular disorder focused, specialty sales forces in North America and, possibly, other markets to effectively support the commercialization of these and future products. We believe that a specialty sales force will be sufficient to target key prescribing physicians in these areas. We currently do not have any sales or marketing capabilities or experience. We will establish the required capabilities within an appropriate time frame ahead of any product approval and commercialization to support a product launch. If we are not able to establish sales and marketing capabilities or are not successful in commercializing our future products, either on our own or through collaborations with Celgene, any future product revenue will be materially adversely affected.

Intellectual Property

Our commercial success depends in part on our ability to obtain and maintain proprietary protection for our protein therapeutics, novel biological discoveries, screening and drug development technology, to operate without infringing on the proprietary rights of others and to prevent others from infringing our proprietary rights. Our policy is to seek to protect our proprietary position by, among other methods, filing U.S. and foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development and implementation of our business. We also rely on trade secrets, know-how, continuing technological innovation and potential in-licensing opportunities to develop and maintain our proprietary position. Additionally, we expect to benefit from a variety of statutory frameworks in the United States, Europe and other countries that relate to the regulation of biosimilar molecules and orphan drug status. These statutory frameworks provide periods of non-patent-based exclusivity for qualifying molecules. See "Government Regulations".

Our patenting strategy is focused on our protein therapeutics. We seek composition-of-matter and method-of-treatment patents for each such protein in key therapeutic areas. We also seek patent protection with respect to companion diagnostic methods and compositions and treatments for targeted patient populations. We have sought patent protection alone or jointly with our collaborators, as dictated by our collaboration agreements.

Our patent estate, on a worldwide basis, includes approximately 75 issued patents and approximately 300 pending patent applications, with pending and issued claims relating to all of our current clinical stage protein therapeutic candidates, sotatercept, ACE-536 and dalantercept. Of these, approximately 20 issued patents cover the nine receptors for the TGF-β superfamily that we have selected as the core focus of our discovery approach. These figures include in-licensed patents and patent applications to which we hold exclusive commercial rights.

Individual patents extend for varying periods of time depending on the date of filing of the patent application or the date of patent issuance and the legal term of patents in the countries in which they are obtained. Generally, patents issued from applications filed in the United States are effective for twenty years from the earliest non-provisional filing date. In addition, in certain instances, a patent term can be extended to recapture a portion of the term effectively lost as a result of the FDA regulatory review period, however, the restoration period cannot be longer than five years and the total

Table of Contents

patent term including the restoration period must not exceed 14 years following FDA approval. The duration of foreign patents varies in accordance with provisions of applicable local law, but typically is also twenty years from the earliest international filing date. Our issued patents with respect to our receptor-focused platform will expire on dates ranging from 2013 to 2018, and, our issued patents and pending applications with respect to our protein therapeutic candidates will expire on dates ranging from 2026 to 2033, exclusive of possible patent term extensions, However, the actual protection afforded by a patent varies on a product by product basis, from country to country and depends upon many factors, including the type of patent, the scope of its coverage, the availability of extensions of patent term, the availability of legal remedies in a particular country and the validity and enforceability of the patent.

National and international patent laws concerning protein therapeutics remain highly unsettled. No consistent policy regarding the patent-eligibility or the breadth of claims allowed in such patents has emerged to date in the United States, Europe or other countries. Changes in either the patent laws or in interpretations of patent laws in the United States and other countries can diminish our ability to protect our inventions and enforce our intellectual property rights. Accordingly, we cannot predict the breadth or enforceability of claims that may be granted in our patents or in third-party patents. The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights. Our ability to maintain and solidify our proprietary position for our drugs and technology will depend on our success in obtaining effective claims and enforcing those claims once granted. We do not know whether any of the patent applications that we may file or license from third parties will result in the issuance of any patents. The issued patents that we own or may receive in the future, may be challenged, invalidated or circumvented, and the rights granted under any issued patents may not provide us with sufficient protection or competitive advantages against competitors with similar technology. Furthermore, our competitors may be able to independently develop and commercialize similar drugs or duplicate our technology, business model or strategy without infringing our patents. Because of the extensive time required for clinical development and regulatory review of a drug we may develop, it is possible that, before any of our drugs can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby reducing any advantage of any such patent. The patent positions for our most advanced programs are summarized below:

Sotatercept Patent Coverage

We hold two issued patents covering the sotatercept composition of matter in the United States, one issued patent in Europe (registered in most countries of the European Patent Convention) and additional patents issued or pending in many other major jurisdictions worldwide, including Japan, China, South Korea, Brazil, Mexico, Russia, Israel and India. The expected expiration date for these composition of matter patents is 2026 plus any extensions of term available under national law.

We hold two issued patents covering the treatment of anemia by administration of sotatercept in the United States and similar patents issued or pending in many other major jurisdictions worldwide, including Europe, Japan, China, South Korea, Brazil, Mexico, Russia, Israel and India. The expected expiration date for these composition of matter patents is 2027 exclusive of possible patent term extensions.

We also hold patents and patent applications directed to a variety of other uses for sotatercept, including the reduction of tumor cell burden in multiple myeloma.

ACE-536 Patent Coverage

We hold two issued patents covering the ACE-536 composition of matter in the United States, and additional patents issued or pending in many other major jurisdictions worldwide, including Europe,

Table of Contents

Japan, China, South Korea, Brazil, Mexico, Russia and India. The expected expiration dates for these composition of matter patents are 2028 and 2029, exclusive of possible patent term extensions.

We hold one issued patent covering the treatment of anemia by administration of ACE-536 in the United States and similar patents issued or pending in other major jurisdictions worldwide, including Europe, Japan, China, South Korea, Brazil, Mexico, Russia and India. The expected expiration date for these method of treatment patents is 2029 exclusive of possible patent term extensions.

Dalantercept Patent Coverage

We hold one issued patent covering the dalantercept composition of matter in the United States, which is expected to expire in 2029, exclusive of possible patent term extensions, and we hold additional pending patent applications. We hold additional issued patents and pending patent applications covering composition of matter in many other major jurisdictions worldwide, including Europe, Japan, China, South Korea, Brazil, Mexico, Russia and India. The expected expiration dates for these patent filings claiming the dalantercept composition of matter, if issued, are either 2027 or 2029, exclusive of possible patent term extensions.

We hold one issued patent covering the treatment of tumor angiogenesis by administration of dalantercept in the United States and similar patents issued or pending in other major jurisdictions worldwide, including Europe, Japan, China, South Korea, Brazil, Mexico, Russia and India. The expected expiration date for these method of treatment patents is 2027, exclusive of possible patent term extensions.

We also hold patent applications directed to a variety of other uses for dalantercept, including the treatment of renal cell carcinoma with a combination of dalantercept and a VEGF-targeted tyrosine kinase inhibitor. This patent application is jointly invented and owned with the Beth Israel Deaconess Medical Center, or BIDMC, and we have secured an exclusive license to the BIDMC rights. The expected expiration date for these patent applications, should they issue as patents, is 2033 plus any extensions of term available under national law.

Trade Secrets

In addition to patents, we rely upon unpatented trade secrets and know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary information, in part, using confidentiality agreements with our commercial partners, collaborators, employees and consultants and invention assignment agreements with our employees. These agreements are designed to protect our proprietary information and, in the case of the invention assignment agreements, to grant us ownership of technologies that are developed through a relationship with a third party. These agreements may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our commercial partners, collaborators, employees and consultants use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

In-Licenses

Effective June 21, 2012, we entered into a license agreement with the Beth Israel Deaconess Medical Center, or BIDMC, to obtain worldwide, exclusive rights under patent filings jointly invented by us and BIDMC. The patent rights relate to the treatment of renal cell cancer by combination therapy with dalantercept and VEGF-receptor tyrosine kinase inhibitors (TKIs). The intellectual property includes one pending U.S. patent filing and one pending PCT (international) patent filing. If issued, the patents are predicted to expire in 2033. Under the agreement, BIDMC retained rights, on behalf of itself and other non-profit academic institutions, to practice under the licensed rights for

Table of Contents

non-profit purposes. The license rights granted to us are further subject to any rights the United States Government may have in such licensed rights due to its sponsorship of research that led to the creation of the licensed rights. We agreed to pay BIDMC specified development and sales milestone payments aggregating up to $1.0 million. In addition, we are required to pay BIDMC royalties in the low single-digits on worldwide net product sales of drug labeled for treatment regimens that are claimed in the licensed patents. The agreement terminates upon the expiration of the last valid claim of the licensed patent rights. We may terminate the agreement at any time by giving BIDMC advance written notice. The agreement may also be terminated by BIDMC in the event of a material breach by us or in the event we become subject to specified bankruptcy or similar circumstances. In any termination event, we retain our joint ownership of the patent rights and a worldwide non-exclusive license with right to sublicense.

In August 6, 2010, we entered into an amended and restated license agreement with the Ludwig Institute for Cancer Research, or LICR, to obtain worldwide, exclusive rights under patent filings solely owned by LICR and patent rights jointly invented by us and LICR. The LICR-owned patent rights relate to the first cloning of the type I activin receptors, ALK1, ALK2, ALK3, ALK4, ALK5 and ALK6, and include claims to nucleic acids, proteins and antibodies with respect to each of the foregoing. These patent rights expire between the years 2013 and 2018. The license excludes the rights with regard to anti-ALK2 antibodies. The joint patent rights relate to the treatment of pancreatic tumors with dalantercept and, if issued, such patent rights are expected to expire in 2029. Under the agreement, LICR retained rights, on behalf of itself and other non-profit academic institutions, to practice under the licensed rights for non-profit purposes. We agreed to pay LICR specified development and sales milestone payments aggregating up to $1.6 million for dalantercept. In addition, we are required to pay LICR royalties in the low single-digits on worldwide net product sales of products claimed in the licensed patents, with royalty obligations continuing at a 50% reduced rate for eight years after patent expiration. If we sublicense the LICR patent rights, we will owe LICR a percentage of sublicensing revenue, excluding payments based on the level of sales, profits or other levels of commercialization. The agreement terminates upon the expiration of royalty obligations. We may terminate the agreement at any time by giving LICR advance written notice. The agreement may also be terminated by LICR in the event of a material breach by us or in the event we become subject to specified bankruptcy or similar circumstances. In any termination we retain our joint ownership right in the jointly owned patent filings.

In August 2010, we entered into two amended and restated license agreements with the Salk Institute for Biological Studies, or Salk, providing rights under U.S. patent filings solely owned by Salk. The agreements for the licensed patent rights relate to the first cloning of the type II activin receptors, human ActRIIA and frog ActRIIB, respectively, and include claims to vertebrate homolog nucleic acids and proteins with respect to each of the foregoing. These patent rights expire between the years 2016 and 2017. One of these agreements relates to ActRIIA and sotatercept; the other agreement relates to ActRIIB, ACE-536 and the discontinued program ACE-031. The licenses granted are exclusive as to the therapeutic products that are covered by the patents and non-exclusive as to diagnostic products and other products that are developed using the Salk patent rights. If we sublicense the Salk patent rights, we will owe Salk a percentage of sublicensing revenue, excluding payments based on sales. Under the agreements, Salk retained rights, on behalf of itself and other non-profit academic institutions, to practice under the licensed rights for non-profit purposes. We agreed to pay Salk specified development milestone payments totaling up to $2.0 million for sotatercept and $0.7 million for ACE-536. In addition, we are required to pay Salk royalties in the low single-digits on worldwide net product sales by us or our sublicensees of products claimed in the licensed patents, or derived from use of the licensed patent rights, with royalty obligations continuing at a reduced rate for a period of time after patent expiration. The agreements terminate upon the expiration of royalty obligations. We may terminate either agreement at any time by giving Salk advance written notice. Either agreement

Table of Contents

may also be terminated by Salk in the event of a material breach by us or in the event we become subject to bankruptcy or similar circumstances.

Government Regulation

The preclinical studies and clinical testing, manufacture, labeling, storage, record keeping, advertising, promotion, export, marketing and sales, among other things, of our protein therapeutic candidates and future products, are subject to extensive regulation by governmental authorities in the United States and other countries. In the United States, pharmaceutical products are regulated by the FDA under the Federal Food, Drug, and Cosmetic Act and other laws, including, in the case of biologics, the Public Health Service Act. We expect sotatercept, ACE-536, and dalantercept to be regulated by the FDA as biologics and to be reviewed by the Center for Drug Evaluation and Research (CDER) as proteins intended for therapeutic use. Protein therapeutics require the submission of a Biologics License Application, or BLA, and approval by the FDA prior to being marketed in the U.S. Manufacturers of protein therapeutics may also be subject to state regulation. Failure to comply with FDA requirements, both before and after product approval, may subject us or our partners, contract manufacturers, and suppliers to administrative or judicial sanctions, including FDA refusal to approve applications, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, fines and/or criminal prosecution.

The steps required before a biologic may be approved for marketing of an indication in the United States generally include:

- completion of preclinical laboratory tests, animal studies and formulation studies conducted according to Good Laboratory Practices, or GLPs, and other applicable regulations;
- submission to the FDA of an Investigational New Drug application or IND, which must become effective before human clinical trials may commence;
- completion of adequate and well-controlled human clinical trials in accordance with Good Clinical Practices, or GCPs, to establish that the biological product is "safe, pure and potent", which is analogous to the safety and efficacy approval standard for a chemical drug product for its intended use;
- submission to the FDA of a BLA;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with applicable current Good Manufacturing Practice requirements, or cGMPs; and
- FDA review of the BLA and issuance of a biologics license which is the approval necessary to market a protein therapeutic.

Preclinical studies include laboratory evaluation of product chemistry, toxicity and formulation as well as animal studies to assess the potential safety and efficacy of the biologic candidate. Preclinical studies must be conducted in compliance with FDA regulations regarding GLPs. The results of the preclinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND. Some preclinical testing may continue even after the IND is submitted. In addition to including the results of the preclinical testing, the IND will also include a protocol detailing, among other things, the objectives of the clinical trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated if the first phase or phases of the clinical trial lends themselves to an efficacy determination. The IND will automatically become effective 30 days after receipt by the FDA, unless the FDA within the 30-day time period places the IND on clinical hold because of its concerns about the drug candidate or the conduct of the trial described in the clinical protocol included in the IND. The IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can proceed.

Table of Contents

All clinical trials must be conducted under the supervision of one or more qualified principal investigators in accordance with GCPs. They must be conducted under protocols detailing the objectives of the applicable phase of the trial, dosing procedures, research subject selection and exclusion criteria and the safety and effectiveness criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND, and progress reports detailing the status of the clinical trials must be submitted to the FDA annually. Sponsors also must timely report to the FDA serious and unexpected adverse reactions, any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator's brochure, or any findings from other studies or animal or in vitro testing that suggest a significant risk in humans exposed to the drug. An institutional review board, or IRB, at each institution participating in the clinical trial must review and approve the protocol before a clinical trial commences at that institution, approve the information regarding the trial and the consent form that must be provided to each research subject or the subject's legal representative, and monitor the study until completed.

Clinical trials are typically conducted in three sequential phases, but the phases may overlap and different trials may be initiated with the same drug candidate within the same phase of development in similar or differing patient populations. Phase 1 trials may be conducted in a limited number of patients, but are usually conducted in healthy volunteer subjects. The drug candidate is initially tested for safety and, as appropriate, for absorption, metabolism, distribution, excretion, pharmacodynamics and pharmacokinetics.

Phase 2 usually involves trials in a larger, but still limited, patient population to evaluate preliminarily the efficacy of the drug candidate for specific, targeted indications to determine dosage tolerance and optimal dosage and to identify possible short-term adverse effects and safety risks.

Phase 3 trials are undertaken to further evaluate clinical efficacy of a specific endpoint and to test further for safety within an expanded patient population at geographically dispersed clinical trial sites. Phase 1, Phase 2, or Phase 3 testing might not be completed successfully within any specific time period, if at all, with respect to any of our protein therapeutic candidates. Results from one trial are not necessarily predictive of results from later trials. Furthermore, the FDA or the sponsor may suspend clinical trials at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug candidate has been associated with unexpected serious harm to patients.

The results of the preclinical studies and clinical trials, together with other detailed information, including information on the manufacture and composition of the product, are submitted to the FDA as part of a BLA requesting approval to market the drug candidate for a proposed indication. Under the Prescription Drug User Fee Act, as re-authorized most recently in July 2012, the fees payable to the FDA for reviewing a BLA, as well as annual fees for commercial manufacturing establishments and for approved products, can be substantial. The fee for review of an application that requires clinical data, such as a BLA, for the one year period ending September 30, 2013, is almost $2.0 million, subject to certain limited deferrals, waivers, and reductions that may be available. The fees typically increase each year. Each BLA submitted to the FDA for approval is reviewed for administrative completeness and reviewability within 60 days following receipt by the FDA of the application. If the BLA is found complete, the FDA will file the BLA, triggering a full review of the application. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the time of submission. The FDA's established goal is to review 90% of priority BLA applications within six months after the application is accepted for filing and 90% of standard BLA applications within 10 months of the acceptance date, whereupon a review decision is to be made. The FDA, however, may not approve a drug candidate within these established goals and its review goals are subject to change from time to time. Further, the outcome of the review, even if generally favorable, may not be an actual approval

Table of Contents

but a "complete response letter" that describes additional work that must be done before the application can be approved. Before approving a BLA, the FDA may inspect the facility or facilities at which the product is manufactured and will not approve the product unless the facility complies with cGMPs. The FDA may deny approval of a BLA if applicable statutory or regulatory criteria are not satisfied, or may require additional testing or information, which can extend the review process. FDA approval of any application may include many delays or never be granted. If a product is approved, the approval may impose limitations on the uses for which the product may be marketed, may require that warning statements be included in the product labeling, may require that additional studies be conducted following approval as a condition of the approval, and may impose restrictions and conditions on product distribution, prescribing, or dispensing in the form of a Risk Evaluation and Mitigation Strategy, or REMS, or otherwise limit the scope of any approval. The FDA must approve a BLA supplement or a new BLA before a product may be marketed for other uses or before certain manufacturing or other changes may be made. Further post-marketing testing and surveillance to monitor the safety or efficacy of a product is required. Also, product approvals may be withdrawn if compliance with regulatory standards is not maintained or if safety or manufacturing problems occur following initial marketing. In addition, new government requirements may be established that could delay or prevent regulatory approval of our protein therapeutic candidates under development.

As part of the recently-enacted Patient Protection and Affordable Care Act of 2010, under the subtitle of Biologics Price Competition and Innovation Act of 2009, or the BPCI, a statutory pathway has been created for licensure, or approval, of biological products that are biosimilar to, and possibly interchangeable with, earlier biological products licensed under the Public Health Service Act. Also under the BPCI, innovator manufacturers of original reference biological products are granted 12 years of exclusivity before biosimilars can be approved for marketing in the United States. The objectives of the BPCI are conceptually similar to those of the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the "Hatch-Waxman Act", which established abbreviated pathways for the approval of drug products. The implementation of an abbreviated approval pathway for biological products is under the direction of the FDA and is currently being developed. In late 2010, the FDA held a hearing to receive comments from a broad group of stakeholders regarding the implementation of the BPCI. Since that hearing in 2010, the FDA, in February 2012 and February 2013, has issued several draft guidances for industry related to the BPCI, addressing scientific, quality and procedural issues relevant to an abbreviated application for a biosimilar product. The approval of a biologic product biosimilar to one of our products could have a material adverse impact on our business as it may be significantly less costly to bring to market and may be priced significantly lower than our products.

Both before and after the FDA approves a product, the manufacturer and the holder or holders of the BLA for the product are subject to comprehensive regulatory oversight. For example, quality control and manufacturing procedures must conform, on an ongoing basis, to cGMP requirements, and the FDA periodically inspects manufacturing facilities to assess compliance with cGMPs. Accordingly, manufacturers must continue to spend time, money and effort to maintain cGMP compliance.

Orphan Drug Act

The Orphan Drug Act provides incentives to manufacturers to develop and market drugs for rare diseases and conditions affecting fewer than 200,000 persons in the United States at the time of application for orphan drug designation. Orphan drug designation must be requested before submitting a BLA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. If a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the holder of the approval is entitled to a seven-year exclusive marketing period in the United States for that product except in very limited circumstances. For example, a drug that the FDA considers to be clinically

Table of Contents

superior to, or different from, another approved orphan drug, even though for the same indication, may also obtain approval in the United States during the seven-year exclusive marketing period. In addition, holders of exclusivity for orphan drugs are expected to assure the availability of sufficient quantities of their orphan drugs to meet the needs of patients. Failure to do so could result in the withdrawal of marketing exclusivity for the drug. ACE-536 has orphan drug designation in the United States for the treatment of β-thalassemia and for the treatment of MDS. The FDA has granted orphan designation for sotatercept for the treatment of β-thalassemia.

Legislation similar to the Orphan Drug Act has been enacted outside the U.S., including in the EU. The orphan legislation in the EU is available for therapies addressing chronic debilitating or life-threatening conditions that affect five or fewer out of 10,000 persons or are financially not viable to develop. The market exclusivity period is for ten years, although that period can be reduced to six years if, at the end of the fifth year, available evidence establishes that the product is sufficiently profitable not to justify maintenance of market exclusivity. The market exclusivity may be extended to 12 years if sponsors complete a pediatric investigation plan agreed upon with the relevant committee of the EMA.

Expedited Review and Approval

The FDA has various programs, including Fast Track, priority review, and accelerated approval, which are intended to expedite or simplify the process for reviewing drugs, and/or provide for the approval of a drug on the basis of a surrogate endpoint. Even if a drug qualifies for one or more of these programs, the FDA may later decide that the drug no longer meets the conditions for qualification or that the time period for FDA review or approval will be shortened. Generally, drugs that are eligible for these programs are those for serious or life-threatening conditions, those with the potential to address unmet medical needs and those that offer meaningful benefits over existing treatments. For example, Fast Track is a process designed to facilitate the development and expedite the review of drugs to treat serious or life- threatening diseases or conditions and fill unmet medical needs. Priority review is designed to give drugs that offer major advances in treatment or provide a treatment where no adequate therapy exists an initial review within six months as compared to a standard review time of ten months. Although Fast Track and priority review do not affect the standards for approval, the FDA will attempt to facilitate early and frequent meetings with a sponsor of a Fast Track designated drug and expedite review of the application for a drug designated for priority review. Accelerated approval provides for an earlier approval for a new drug that is intended to treat a serious or life-threatening disease or condition and that fills an unmet medical need based on a surrogate endpoint. A surrogate endpoint is a laboratory measurement or physical sign used as an indirect or substitute measurement representing a clinically meaningful outcome. As a condition of approval, the FDA may require that a sponsor of a drug candidate receiving accelerated approval perform post-marketing clinical trials to confirm the clinically meaning full outcome as predicted by the surrogate marker trial.

In the Food and Drug Administration Safety and Innovation Act, or FDASIA, which was signed into law in July 2012, Congress encouraged the FDA to utilize innovative and flexible approaches to the assessment of products under accelerated approval. The law required the FDA to issue related draft guidance within a year after the law's enactment and also promulgate confirming regulatory changes. In June 2013, the FDA published a draft Guidance for Industry entitled, "Expedited Programs for Serious Conditions Drugs and Biologics" which provides guidance on FDA programs that are intended to facilitate and expedite development and review of new drugs as well as threshold criteria generally applicable to concluding that a drug is a candidate for these expedited development and review programs. In addition to the Fast Track, accelerated approval and priority review programs discussed above, the FDA also provided guidance on a new program for Breakthrough Therapy designation. A request for Breakthrough Therapy designation should be submitted concurrently with, or

Table of Contents

as an amendment to an IND. FDA has already granted this designation to over 30 new drugs and recently approved a couple of Breakthrough Therapy designated drugs.

Pediatric Exclusivity and Pediatric Use

Under the Best Pharmaceuticals for Children Act, or BPCA, certain drugs may obtain an additional six months of exclusivity, if the sponsor submits information requested in writing by the FDA, or a Written Request, relating to the use of the active moiety of the drug in children. The FDA may not issue a Written Request for studies on unapproved or approved indications or where it determines that information relating to the use of a drug in a pediatric population, or part of the pediatric population, may not produce health benefits in that population.

We have not received a Written Request for such pediatric studies, although we may ask the FDA to issue a Written Request for such studies in the future. To receive the six-month pediatric market exclusivity, we would have to receive a Written Request from the FDA, conduct the requested studies in accordance with a written agreement with the FDA or, if there is no written agreement, in accordance with commonly accepted scientific principles, and submit reports of the studies. A Written Request may include studies for indications that are not currently in the labeling if the FDA determines that such information will benefit the public health. The FDA will accept the reports upon its determination that the studies were conducted in accordance with and are responsive to the original Written Request or commonly accepted scientific principles, as appropriate, and that the reports comply with the FDA's filing requirements.

In addition, the Pediatric Research Equity Act, or PREA, requires a sponsor to conduct pediatric studies for most drugs and biologicals, for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, original NDAs, BLAs and supplements thereto must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must include the evaluation of the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor or FDA may request a deferral of pediatric studies for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug or biologic is ready for approval for use in adults before pediatric studies are complete or that additional safety or effectiveness data needs to be collected before the pediatric studies begin. After April 2013, the FDA must send a non-compliance letter to any sponsor that fails to submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation.

As part of the FDASIA, Congress made a few revisions to BPCA and PREA, which were slated to expire on September 30, 2012, and made both laws permanent.

Reimbursement

In both domestic and foreign markets, sales and reimbursement of any approved products will depend, in part, on the extent to which the costs of such products will be covered by third-party payors, such as government health programs, commercial insurance and managed healthcare organizations. These third-party payors are increasingly challenging the prices charged for medical products and services and imposing controls to manage costs. The containment of healthcare costs has become a priority of federal and state governments and the prices of drugs have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. In addition, there is significant uncertainty regarding the reimbursement status of newly approved

Table of Contents

healthcare products. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the cost-effectiveness of our products. If third-party payors do not consider our products to be cost-effective compared to other therapies, the payors may not cover our products after approved as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis.

Within the United States, if we obtain appropriate approval in the future to market any of our current protein therapeutic candidates, we may seek approval and coverage for those products under Medicaid, Medicare and the Public Health Service (PHS) pharmaceutical pricing program and also seek to sell the products to federal agencies.

Medicaid is a joint federal and state program that is administered by the states for low income and disabled beneficiaries. Under the Medicaid Drug Rebate Program, manufacturers are required to pay a rebate for each unit of product reimbursed by the state Medicaid programs. The amount of the rebate for each product is set by law and may be subject to an additional discount if certain pricing increases more than inflation.

Medicare is a federal program administered by the federal government that covers individuals age 65 and over as well as those with certain disabilities. Medicare Part D provides coverage to enrolled Medicare patients for self-administered drugs (i.e., drugs that do not need to be administered by a physician). Medicare Part D is administered by private prescription drug plans approved by the U.S. government and each drug plan establishes its own Medicare Part D formulary for prescription drug coverage and pricing, which the drug plan may modify from time-to-time.

Medicare Part B covers most injectable drugs given in an in-patient setting, and some drugs administered by a licensed medical provider in hospital outpatient departments and doctors offices. Medicare Part B is administered by Medicare Administrative Contractors, which generally have the responsibility of making coverage decisions. Subject to certain payment adjustments and limits, Medicare generally pays for Part B covered drugs based on a percentage of manufacturer-reported average sales price.

Drug products are subject to discounted pricing when purchased by federal agencies via the Federal Supply Schedule (FSS). FFS participation is required for a drug product to be covered and paid for by certain federal agencies and for coverage under Medicaid, Medicare Part B and the PHS pharmaceutical pricing program. FSS pricing is negotiated periodically with the Department of Veterans Affairs. FSS pricing is intended to not exceed the price that a manufacturer charges its most-favored non-federal customer for its product. In addition, prices for drugs purchased by the Veterans Administration, Department of Defense (including drugs purchased by military personnel and dependents through the TRICARE retail pharmacy program), Coast Guard, and PHS are subject to a cap on pricing (known as the "federal ceiling price") and may be subject to an additional discount if pricing increases more than inflation.

To maintain coverage of drugs under the Medicaid Drug Rebate Program, manufacturers are required to extend discounts to certain purchasers under the PHS pharmaceutical pricing program. Purchasers eligible for discounts include hospitals that serve a disproportionate share of financially needy patients, community health clinics and other entities that receive health services grants from the PHS.

The American Recovery and Reinvestment Act of 2009 provides funding for the federal government to compare the effectiveness of different treatments for the same illness. A plan for the research will be developed by the Department of Health and Human Services, the Agency for Healthcare Research and Quality and the National Institutes for Health, and periodic reports on the status of the research and related expenditures will be made to Congress. Although the results of the comparative effectiveness studies are not intended to mandate coverage policies for public or private

Table of Contents

payors, it is not clear what effect, if any, the research will have on the sales of any product, if any such product or the condition that it is intended to treat is the subject of a study. It is also possible that comparative effectiveness research demonstrating benefits in a competitor's product could adversely affect the sales of any of our approved protein therapeutics. If third-party payors do not consider our products to be cost-effective compared to other available therapies, they may not cover our products as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis.

The United States and state governments continue to propose and pass legislation designed to reduce the cost of healthcare. In March 2010, the United States Congress enacted the Patient Protection and Affordable Care Act and the Health Care and Education Reconciliation Act which includes changes to the coverage and payment for drug products under government health care programs. Adoption of other new legislation at the federal or state level could further limit reimbursement for pharmaceuticals.

Outside the United States, ensuring adequate coverage and payment for our products will face challenges. Pricing of prescription pharmaceuticals is subject to governmental control in many countries. Pricing negotiations with governmental authorities can extend well beyond the receipt of regulatory marketing approval for a product and may require us to conduct a clinical trial that compares the cost effectiveness of our protein therapeutic candidates or products to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in our commercialization efforts. Third-party payors are challenging the prices charged for medical products and services, and many third-party payors limit reimbursement for newly-approved health care products. Recent budgetary pressures in many European Union countries are also causing governments to consider or implement various cost-containment measures, such as price freezes, increased price cuts and rebates. If budget pressures continue, governments may implement additional cost-containment measures. Cost-control initiatives could decrease the price we might establish for products that we may develop or sell, which would result in lower product revenues or royalties payable to us. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products.

Foreign Regulation

In addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our protein therapeutic candidates. Whether or not we obtain FDA approval for a protein therapeutic candidate, we must obtain approval from the comparable regulatory authorities of foreign countries or economic areas, such as the European Union, before we may commence clinical trials or market products in those countries or areas. The approval process and requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from place to place, and the time may be longer or shorter than that required for FDA approval.

Certain countries outside of the United States have a process that requires the submission of a clinical trial application much like an IND prior to the commencement of human clinical trials. In Europe, for example, a clinical trial application, or CTA, must be submitted to the competent national health authority and to independent ethics committees in each country in which a company intends to conduct clinical trials. Once the CTA is approved in accordance with a country's requirements, clinical trial development may proceed in that country. In all cases, the clinical trials must be conducted in accordance with good clinical practices, or GCPs and other applicable regulatory requirements.

Under European Union regulatory systems, a company may submit marketing authorization applications either under a centralized or decentralized procedure. The centralized procedure is compulsory for medicinal products produced by biotechnology or those medicinal products containing

Table of Contents

new active substances for specific indications such as the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, viral diseases and designated orphan medicines, and optional for other medicines which are highly innovative. Under the centralized procedure, a marketing application is submitted to the European Medicines Agency where it will be evaluated by the Committee for Medicinal Products for Human Use and a favorable opinion typically results in the grant by the European Commission of a single marketing authorization that is valid for all European Union member states within 67 days of receipt of the opinion. The initial marketing authorization is valid for five years, but once renewed is usually valid for an unlimited period. The decentralized procedure provides for approval by one or more "concerned" member states based on an assessment of an application performed by one member state, known as the "reference" member state. Under the decentralized approval procedure, an applicant submits an application, or dossier, and related materials to the reference member state and concerned member states. The reference member state prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. Within 90 days of receiving the reference member state's assessment report, each concerned member state must decide whether to approve the assessment report and related materials. If a member state does not recognize the marketing authorization, the disputed points are eventually referred to the European Commission, whose decision is binding on all member states.

As in the United States, we may apply for designation of a product as an orphan drug for the treatment of a specific indication in the European Union before the application for marketing authorization is made. Orphan drugs in Europe enjoy economic and marketing benefits, including up to 10 years of market exclusivity for the approved indication unless another applicant can show that its product is safer, more effective or otherwise clinically superior to the orphan designated product.

Additional Regulation

We are also subject to regulation under the Occupational Safety and Health Act, the Environmental Protection Act, the Toxic Substances Control Act, the Resource Conservation and Recovery Act and other present and potential federal, state or local regulations. These and other laws govern our use, handling and disposal of various biological and chemical substances used in, and waste generated by our operations. Our research and development involves the controlled use of hazardous materials, chemicals and viruses. Although we believe that our safety procedures for handling and disposing of such materials comply with the standards prescribed by state and federal regulations, the risk of accidental contamination or injury from these materials cannot be completely eliminated. In the event of such an accident, we could be held liable for any damages that result and any such liability could exceed our resources.

There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biological products, government control and other changes to the healthcare system of the U.S. It is uncertain what legislative proposals will be adopted or what actions federal, state or private payers for medical goods and services may take in response to any healthcare reform proposals or legislation. We cannot predict the effect medical or healthcare reforms may have on our business, and no assurance can be given that any such reforms will not have a material adverse effect.

Manufacturing

We currently manufacture drug substance for our preclinical studies, Phase 1 clinical trials and Phase 2 clinical trials of ACE-536 and dalantercept. We manufacture material compliant to U.S. and European cGMP at our 12,000 square foot multi-product facility located at our corporate headquarters in Cambridge, Massachusetts. We have the capabilities to manufacture receptor fusion proteins, monoclonal antibodies, and other protein therapeutics.

Table of Contents

Our manufacturing facility is based on single use, disposable technology to maximize the focus of personnel and other resources on the production process, minimizing the need for cleaning and sterilization while optimizing the efficiency of product change-over. The facility consists of four independent clean rooms totaling 4,000 square feet. The facility includes one 250 liter and one 1,000 liter single use bioreactor and has space for two additional 1,000 liter bioreactors.

Approximately 20 fulltime employees focus on our process development and manufacturing activities. We believe that our strategic investment in manufacturing capabilities allows us to advance our protein therapeutic candidates at a more rapid pace and provides us with more portfolio flexibility than if we used a contract manufacturer. The facility produces drug substance in a cost-effective manner while allowing us to retain control over the process and provides an ability to balance the requirements of multiple programs and avoid costly commitments of funds before clinical data are available.

Our manufacturing capabilities encompass the full manufacturing process through quality control and quality assurance. These groups are integrated with our project teams from discovery through development. This structure enables us to efficiently transfer research stage lead molecules into manufacturing. We have designed our manufacturing facility and processes to provide maximum flexibility and rapid change over for the manufacture of different protein therapeutic candidates. We outsource fill-finish, packaging, labeling, shipping, and distribution.

We manufacture our protein therapeutic candidates using readily available raw materials and well established manufacturing procedures based on a standardized process modified for each of our protein therapeutic candidates. We produce our proteins in bioreactors using Chinese hamster ovary cells that have been genetically engineered to produce our specific protein therapeutic candidates. We then purify the proteins using industry standard methods, which include affinity chromatography and ultrafiltration operations. Processes developed within our facility have been successfully transferred to commercial facilities based on stainless steel bioreactors. We have conducted comparability characterization on sotatercept between our Phase 2 material and material made at a commercial manufacturer and found them to be comparable.

We believe that we can scale our manufacturing processes to support our clinical development programs and the potential commercialization of our protein therapeutic candidates. For our early phase protein therapeutic candidates, we intend to continue to manufacture drug substance for preclinical testing and Phase 1 and Phase 2 clinical development at our current facilities. As ACE-536 progresses to Phase 3 clinical trials, we intend to transfer the process for Phase 3 production to Celgene, under the terms of our collaboration agreements. We have already successfully transferred the manufacturing process for sotatercept to Celgene, and we expect Celgene will use a contract manufacturer for Phase 3 and commercial supply of sotatercept and ACE-536. We intend to contract with a third party manufacturer for the supply of dalantercept for Phase 3 clinical trials.

Employees

As of September 30, 2013, we had 78 full-time employees, 62 of whom are involved in research, development or manufacturing, and 20 of whom have Ph.D. or M.D. degrees. We have no collective bargaining agreements with our employees and we have not experienced any work stoppages. We consider our relations with our employees to be good.

Facilities

Our corporate, research and development, manufacturing, and clinical trial operations are located in Cambridge, Massachusetts. We lease approximately 94,500 square feet of office and laboratory space in three adjacent buildings with aggregate monthly net-rent expense of approximately $0.4 million. We have sublet approximately 20,000 square feet of space in one of our leased buildings. Two leases expire