

ACCELERON PHARMA INC
Form 10-K
February 25, 2016
Table of Contents

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549
FORM 10-K
(Mark One)

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

For the Fiscal Year Ended December 31, 2015

OR

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

For the Transition Period from _____ to _____

Commission File Number: 001-36065

ACCELERON PHARMA INC.

(Exact name of Registrant as specified in its charter)

Delaware

27-0072226

(State or other jurisdiction of
incorporation or organization)

(I.R.S. Employer
Identification No.)

128 Sidney Street

02139

Cambridge, Massachusetts

(Zip Code)

(Address of principal executive offices)

(617) 649-9200

(Registrant's telephone number, including area code)

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

Title of Class:

Name of Each Exchange on Which Registered

Common Stock, \$0.001 par value

NASDAQ Global Market

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

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

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

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

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

Edgar Filing: ACCELERON PHARMA INC - Form 10-K

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

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

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

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

The aggregate market value of the registrant's voting and non-voting common stock held by non-affiliates of the registrant (without admitting that any person whose shares are not included in such calculation is an affiliate) computed by reference to the price at which the common stock was last sold (based on the closing share price as quoted on the NASDAQ Global Market) as of the last business day of the registrant's most recently completed second fiscal quarter was approximately \$775 million.

As of January 31, 2016, the registrant had 37,096,412 shares of Common Stock, \$0.001 par value per share, outstanding.

Table of Contents

DOCUMENTS INCORPORATED BY REFERENCE

The following documents (or parts thereof) are incorporated by reference into the following parts of this Form 10-K: Certain information required in Part III of this Annual Report on Form 10-K is incorporated from the Registrant's Proxy Statement for the Annual Meeting of Stockholders to be held on June 2, 2016.

Table of ContentsACCELERON PHARMA INC.
FORM 10-K
INDEX

	Page
<u>PART I</u>	
<u>Item 1. Business</u>	<u>2</u>
<u>Item 1A. Risk Factors</u>	<u>23</u>
<u>Item 1B. Unresolved Staff Comments</u>	<u>44</u>
<u>Item 2. Properties</u>	<u>44</u>
<u>Item 3. Legal Proceedings</u>	<u>44</u>
<u>Item 4. Mine Safety Disclosures</u>	<u>44</u>
<u>PART II</u>	
<u>Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities</u>	<u>45</u>
<u>Item 6. Selected Financial Data</u>	<u>46</u>
<u>Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations</u>	<u>49</u>
<u>Item 7A. Quantitative and Qualitative Disclosures About Market Risk</u>	<u>63</u>
<u>Item 8. Financial Statements and Supplementary Data</u>	<u>63</u>
<u>Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure</u>	<u>63</u>
<u>Item 9A. Controls and Procedures</u>	<u>63</u>
<u>Item 9B. Other Information</u>	<u>65</u>
<u>PART III</u>	
<u>Item 10. Directors, Executive Officers and Corporate Governance</u>	<u>66</u>
<u>Item 11. Executive Compensation</u>	<u>66</u>
<u>Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters</u>	<u>66</u>
<u>Item 13. Certain Relationships and Related Transactions, and Director Independence</u>	<u>66</u>
<u>Item 14. Principal Accounting Fees and Services</u>	<u>66</u>
<u>PART IV</u>	
<u>Item 15. Exhibits and Financial Statement Schedules</u>	<u>67</u>

Table of Contents

FORWARD-LOOKING STATEMENTS

This Annual Report filed on Form 10-K and the information incorporated herein by reference includes statements that are, or may be deemed, "forward-looking statements." In some cases, these forward-looking statements can be identified by the use of forward-looking terminology. The terms "anticipate", "believe", "contemplate", "continue", "could", "estimate", "expect", "forecast", "goal", "intend", "may", "plan", "potential", "predict", "project", "should", "strategy", "target", "will", "would", "vision", or, in each case, the negative or other variations thereon 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 Annual Report on Form 10-K include, among other things, statements regarding our intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things:

- our ongoing and planned preclinical studies and clinical trials;
- clinical trial data and 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 luspatercept and sotatercept;
- 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 therapeutic candidates;
- the rate and degree of market acceptance and clinical utility of any approved therapeutic candidate, particularly in specific patient populations;
- our ability to quickly and efficiently identify and develop therapeutic candidates;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our intellectual property position; and
- our estimates regarding our results of operations, financial condition, liquidity, capital requirements, prospects, growth and strategies.

By their nature, forward-looking statements involve risks and uncertainties because they relate to events, competitive dynamics, and industry change and depend on the economic circumstances that may or may not occur in the future or may occur on longer or shorter timelines than anticipated. We caution you that forward-looking statements are not guarantees of future performance and that our actual results of operations, financial condition and liquidity, and events in the industry in which we operate may differ materially from the forward-looking statements contained herein.

Any forward-looking statements that we make in this Annual Report on Form 10-K speak only as of the date of such statement, and we undertake no obligation to update such statements to reflect events or circumstances after the date of this Annual Report on Form 10-K or to reflect the occurrence of unanticipated events.

You should also read carefully the factors described in the "Risk Factors" section of this Annual Report on Form 10-K to better understand the risks and uncertainties inherent in our business and underlying any forward-looking statements. You are advised, however, to consult any further disclosures we make on related subjects in our Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, press releases, and our website.

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 report are the property of their respective owners. The trademarks that we own include Acceleron Pharma® and IntelliTrap™. Solely for convenience, some of the trademarks, service marks and trade names referred to in this report 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

PART I

Item 1. Business

We are a clinical stage biopharmaceutical company focused on the discovery, development and commercialization of novel therapeutic candidates that are based on the mechanisms that the human body uses to regulate the growth and repair of its cells and tissues. Our research focuses on key natural regulators of cellular growth and repair, particularly the Transforming Growth Factor-Beta, or TGF-beta, protein superfamily. We are a leading company in discovering and developing therapeutic candidates that regulate cellular growth and repair. By combining our discovery and development expertise, including our proprietary knowledge of the TGF-beta superfamily, and our internal protein engineering and manufacturing capabilities, we have built a highly productive discovery and development platform that has generated innovative therapeutic candidates with novel mechanisms of action. These differentiated therapeutic candidates have the potential to significantly improve clinical outcomes for patients across many fields of medicine, and we have focused our discovery and development efforts on treatments for cancer and rare diseases.

We have four internally discovered therapeutic candidates that are currently in clinical trials: luspatercept, sotatercept, dalantercept and ACE-083.

Luspatercept, our lead program, and sotatercept, are partnered with Celgene Corporation, or Celgene. Luspatercept is designed to promote red blood cell production through a novel mechanism, and we are developing luspatercept with Celgene to treat anemia and associated complications in myelodysplastic syndromes (MDS) and beta-thalassemia. In 2015, Celgene initiated two Phase 3 clinical trials for luspatercept for the treatment of MDS and beta-thalassemia. We and Celgene are developing sotatercept to treat patients with chronic kidney disease. Sotatercept has the potential to treat several complications of chronic kidney disease including mineral-bone disorder, vascular calcification and anemia. Celgene is responsible for paying 100% of the development costs for all clinical trials for luspatercept and sotatercept, including our ongoing earlier stage clinical trials for these therapeutic candidates. We may receive up to an additional \$560 million of potential development, regulatory and commercial milestone payments and, if these therapeutic candidates are commercialized, we will receive a royalty on net sales in the low-to-mid 20% range. We will co-promote luspatercept and sotatercept, if approved, in North America for which our commercialization costs will be entirely funded by Celgene.

We wholly own dalantercept and ACE-083, and we are independently developing these therapeutic candidates. We are currently evaluating dalantercept in a Phase 2 clinical trial for the treatment of patients with renal cell carcinoma. ACE-083 is designed for the treatment of focal muscle disorders, such as facioscapulohumeral dystrophy, and we are currently conducting a Phase 1 clinical trial with ACE-083 in healthy volunteers. In 2015, we reported data from the Phase 1 clinical trial of ACE-083 showing marked increases in the volume of muscles treated with ACE-083.

In addition to our clinical programs, we are conducting research to identify new therapeutic candidates to bring forward into clinical trials. To this end, in 2015 we implemented a new platform technology, IntelliTrap™ that is accelerating our discovery efforts. We have nominated an IntelliTrap™ molecule, ACE-2494, as a candidate for clinical development and will initiate IND-enabling activities in 2016. ACE-2494 is designed to treat systemic muscle disorders.

As of December 31, 2015 our operations have been funded primarily by \$105.1 million in equity investments from venture investors, \$219.3 million from public investors, \$64.2 million in equity investments from our collaboration partners and \$233.5 million in upfront payments, milestones, and net research and development payments from our collaboration partners. We estimate that we have spent approximately \$145.4 million on research and development for the three year period from 2013 through 2015.

Our Objectives for the Year 2016

By building on the milestones achieved in 2015, we intend to advance and expand our pipeline in 2016 and achieve the following objectives:

• Luspatercept in Rare Blood Disorders

Continue Phase 3 trials with Celgene for the treatment of myelodysplastic syndromes, the “MEDALIST” trial and beta-thalassemia, the “BELIEVE” trial;

Report updated results from Phase 2 extension study trials in MDS and beta-thalassemia at major medical conferences during the year; and

Announce initial preliminary Phase 2 data in ring sideroblast negative and erythropoiesis stimulating agent naïve MDS patients by year-end.

▲ACE-083 and ACE-2494 in Muscle Disorders

Report additional ACE-083 data from Phase 1 trial;

2

Table of Contents

Initiate ACE-083 Phase 2 trial in facioscapulohumeral muscular dystrophy in the second half of 2016; and
File an IND with the FDA for systemically-acting muscle agent, ACE-2494, by year-end.

Dalantercept in Renal Cell Carcinoma

Announce top-line progression-free survival (PFS) results from Phase 2 DART study in renal cell carcinoma patients.

Sotatercept in Chronic Kidney Disease

Provide update on development strategy in pre-dialysis chronic kidney disease patients in the second half of 2016.

The Acceleron Discovery Platform: Novel Approaches to Potent Biology

Since our founding, we have focused on developing therapeutic candidates that regulate cellular growth and repair.

We have targeted a group of approximately 30 secreted proteins, or ligands, that are collectively referred to as the TGF-beta 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-beta 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-beta superfamily and its receptors, we have generated our novel IntelliTrap™ platform technology and a robust pipeline of innovative clinical and preclinical therapeutic candidates targeting key mechanisms underlying cancer and rare diseases. Additionally, we are conducting a multi-target antibody discovery collaboration with Adimab LLC, or Adimab, a leading antibody discovery company, under which Adimab is generating human antibodies against undisclosed targets that we select. We expect that this collaboration will expand our biologics platform and provide us with enhanced access to antibody therapeutic candidates.

We use our integrated platform of research, development and manufacturing technologies to rapidly and cost-effectively create, test and advance our 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.

Table of Contents

Our Product Pipeline

Luspatercept

Luspatercept is designed to promote red blood cell production through a novel mechanism. We are developing luspatercept, through our collaborations with Celgene, as a treatment for anemia and associated complications in diseases in which erythropoiesis-stimulating agents are either not approved or are not well-suited to treat the underlying anemia, such as beta-thalassemia and MDS.

MDS

With respect to MDS, both our and Celgene's objective is to develop luspatercept as a treatment to increase hemoglobin levels and decrease red blood cell transfusion burden, with patients ultimately becoming transfusion independent.

MDS is 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. Although MDS patients may have varying forms of the disease, 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./EU prevalence at approximately 125,000 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 70% of the MDS patients in the U.S. and EU are classified as lower risk and 30% are classified as higher risk. High risk patients are typically treated with inhibitors of DNA methyltransferase such as Vidaza® or Dacogen®, or generic versions that are now available in some countries. The patients categorized as low risk typically receive erythropoiesis stimulating agents as first-line therapy, though erythropoiesis stimulating agents are not approved by the FDA or the EMA for the 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. After failure on erythropoiesis stimulating agents, patients are treated with red blood cell transfusion and/or Revlimid®, Vidaza® or Dacogen®. Across the disease, approximately 15% of patients have a specific chromosomal mutation and are treated with Revlimid® (2015 U.S. sales of \$152 million for MDS).

Table of Contents

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-beta superfamily, which signaling inhibits red blood cell maturation. For this reason we believe that blocking this excess signaling by luspatercept 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.

Given the effects of members of the TGF-beta superfamily ligands on late-stage erythropoiesis, we have investigated our candidate therapeutics in mouse models of MDS, with a focus on luspatercept. In our 2014 publication in the journal *Nature Medicine*, we and our collaborators showed that the ligand GDF11 is expressed at an elevated level in a mouse model of MDS, leading to elevated levels of an activated transcription factor, P-SMAD2/3, and ineffective erythropoiesis. Treatment with a mouse version of luspatercept, referred to as RAP-536, reduced P-SMAD2/3 levels and caused 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.

In December 2015, Celgene initiated a Phase 3 clinical trial with luspatercept in patients with very low, low and intermediate risk MDS per the Revised International Prognostic Scoring System, the "MEDALIST" trial. The MEDALIST trial targets patients with very low, low or intermediate risk MDS with ring sideroblasts who require RBC transfusions. The trial is double-blinded, placebo-controlled and will enroll an estimated 210 patients randomized 2:1, luspatercept versus placebo. In order to enroll in the trial, patients must be: refractory / intolerant to prior erythropoiesis stimulating agents (ESA) or ESA ineligible, ring sideroblast positive, receive a transfusion of at least 2 units of RBCs every 8 weeks confirmed for a minimum of 16 weeks with no consecutive 8-week period free from transfusion, and no prior lenalidomide, hypomethylating agents or immunosuppressive therapy. Patients are excluded from the study if they have del(5q) or secondary MDS. The primary endpoint for efficacy analysis will be the proportion of patients who become RBC-transfusion independent for a period of at least 8 weeks during the first 24 weeks of treatment.

In addition to the Phase 3 clinical trial, we are currently conducting two Phase 2 clinical trials of luspatercept in patients with MDS. The first clinical trial is designed as a two-part trial, with an ascending dose part to evaluate the safety and efficacy in patients with low or intermediate risk MDS per the International Prognostic Scoring System, and an expansion part in which additional patients are enrolled at a selected dose level (3-month base study). We have currently completed enrollment in all of the dose escalation cohorts and we have completed enrollment of patients in the initial expansion cohort of the trial for a total of 58 patients. We have expanded the trial to include two additional cohorts of patients to further evaluate the effects of luspatercept in selected MDS patient populations. All patients enrolled in the base study are eligible to enroll in a second Phase 2 trial (extension study) that permits dosing with luspatercept for up to an additional two years. These trials are being conducted at sites in Germany.

We believe that preliminary results from the long-term Phase 2 MDS extension study are encouraging. We presented these results, using a data cut-off date of August 31, 2015, at the 57th American Society of Hematology (ASH) Annual Meeting and Exposition in December 2015. As of the cut-off date, a total of 32 patients were treated in the extension study in which luspatercept was administered subcutaneously once every 3 weeks. Of these 32 patients, 13 had a low red blood cell (RBC) transfusion burden (LTB; < 4 units RBC/8 weeks) and 19 had a high transfusion burden (HTB; ≥4 units RBC/8 weeks). 59% of patients had been treated previously with erythropoiesis stimulating agents (ESA) and 19% of patients had previously been treated with lenalidomide. With regard to LTB patients, 9 of 13 (69%) LTB patients achieved the International Working Group (IWG) Hematologic Improvement Erythroid (HI-E) response criterion of a hemoglobin increase ≥1.5 g/dL for ≥8 weeks. With regard to HTB patients, 13 of 19 (68%) HTB patients achieved the IWG HI-E criterion of a reduction of ≥4 units RBC over 8 weeks, and 8 of 19 (42%) HTB patients treated with luspatercept achieved RBC transfusion independence for ≥8 weeks. An additional 3 of 3 (100%) LTB patients with 2 units/8 weeks at baseline achieved RBC transfusion independence for ≥8 weeks. A substantial majority of the patients in the Phase 2 trial had a bone marrow cell morphology referred to as ring sideroblasts and given the

encouraging response rates in these patients, the Phase 3 trial has been designed to focus on patients with this particular cellular morphology. The most common adverse events observed in this extension study, which may be related to luspatercept, were bone pain, headache, hypotonia, myalgia and nausea. There were no drug-related serious adverse events.

Beta-thalassemia

With respect to beta-thalassemia, both our and Celgene's objective is to develop luspatercept as a treatment to increase hemoglobin levels, decrease transfusion burden, decrease iron overload, improve symptoms associated with anemia, and alleviate other disease complications, such as leg ulcers.

Table of Contents

The beta-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 alpha-subunits and two beta-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, alpha-thalassemia and beta-thalassemia, depending on whether the genetic defect lies in the gene encoding the alpha-subunit or the beta-subunit. Beta-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 beta-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 beta-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. Beta-thalassemia is treated primarily by red blood cell transfusions that, over time, cause a toxic accumulation of iron in the body. A central challenge for managing patients with beta-thalassemia is to restore the red blood cell levels while avoiding iron overload. Iron chelation therapy alone costs between \$40,000 and \$60,000 per year in countries such as the United States and Italy 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.

No drug is approved to treat the anemia of beta-thalassemia. Hematopoietic stem cell transplantation is viewed as the only curative approach for beta-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.

Given the effects of members of the TGF-beta superfamily ligands on late-stage erythropoiesis, we have investigated our candidate therapeutics in mouse models of this disease. We evaluated the effects of RAP-536 in a series of studies using a mouse model of beta-thalassemia. These mice carry deletion mutations in the beta-globin genes, resulting in a deficiency of beta-globin protein and hematologic abnormalities very similar to those seen in human beta-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. As reported in our 2014 publication in the journal *Blood*, RAP-536 treatment improved numerous hematologic parameters in these mice, including a decrease in hemoglobin aggregates, 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. Importantly, RAP-536 decreased the elevated levels of the activated transcription factor, P-SMAD2/3, restored iron homeostasis and 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.

In December 2015, Celgene initiated a Phase 3 clinical trial with luspatercept in regularly transfused patients with beta-thalassemia, the "BELIEVE" trial. The BELIEVE trial targets adult beta-thalassemia patients who are regularly transfused. The trial is double-blinded and placebo-controlled and will enroll an estimated 300 patients randomized 2:1, luspatercept versus placebo. In order to enroll in the trial, patients must receive 6-20 units RBC transfused over the prior 24 weeks and have no transfusion-free period \geq 35 days. Patients will be monitored for a 12-week prospective pre-treatment period to calculate baseline transfusion burden. The primary endpoint for efficacy analysis will be the proportion of patients with at least a 33% reduction in transfusion burden during weeks 13 to 24 of the trial compared to the 12 weeks preceding treatment.

In addition to the Phase 3 clinical trial, we are currently conducting two Phase 2 clinical trials of luspatercept in patients with beta-thalassemia. The first clinical trial is designed as a two-part trial, with an ascending dose part to evaluate the safety and efficacy of luspatercept in patients with beta-thalassemia, and an expansion part in which additional patients are enrolled at a selected dose level (3-month base study). We have currently completed enrollment and treatment of all of the dose escalation cohorts as well as the expansion cohort of the trial. Patients enrolled in the

initial 3-month trial are eligible to enroll in a second Phase 2 trial (extension study) that permits dosing with luspatercept for up to an additional two years. This trial is currently being conducted at sites in Italy and Greece. We believe the preliminary results from the Phase 2 clinical trials are encouraging. We presented these results, using a data cut-off date of September 25, 2015, at the 57th ASH Annual Meeting and Exposition in December 2015. As of the cut-off date, a total of 64 patients were treated in the dose escalation and expansion cohorts of this study, in which luspatercept was administered subcutaneously, once every 3 weeks. A total of 59 patients were evaluable for efficacy (5 patients were ongoing with <12 weeks treatment). Of these 59 patients, 31 were non-transfusion dependent and 28 were transfusion dependent. Specifically, 22 of 28 (79%) transfusion dependent patients had a $\geq 20\%$ reduction in transfusion burden, 21 of 28 (75%) had a $\geq 33\%$ reduction, and 16 of 28 (57%) had a $\geq 50\%$ reduction over a 12-week period.

Table of Contents

A trend of reduction in liver iron concentration, or LIC, was observed in the majority of non-transfusion dependent patients with or without iron chelation therapy, and in the majority of transfusion dependent patients receiving iron chelation therapy. Improvement in quality of life in non-transfusion dependent patients correlated with increase in hemoglobin. Rapid healing of leg ulcers, a serious complication of beta-thalassemia, was observed in 3 patients, with 2 additional patients experiencing partial healing. The most common related adverse events were bone pain, myalgia, headache, arthralgia, musculoskeletal pain, asthenia, injection site pain, back pain and pain in jaw. There were no drug-related serious adverse events. 6 of 59 (10%) patients discontinued early with an associated adverse event: bone pain (2 patients) and arthralgia, asthenia, cerebrovascular accident and headache (1 patient each).

Sotatercept

We and Celgene are developing sotatercept for the treatment of chronic kidney disease, or CKD, a disorder characterized by anemia and a mineral and bone disorder that leads to bone loss and cardiovascular disease. The mineral and bone disorder in these patients is not well-managed with current therapies. Studies in mice show that sotatercept may have beneficial effects on fibrotic damage to the kidney and on the development of calcified deposits that may contribute to the elevated risk of heart vascular disease in CKD patients. Data from our ongoing Phase 2 clinical trial in patients with end-stage kidney disease shows that sotatercept may have beneficial effects on the mineral and bone disorder in these patients and may decrease the accumulation of vascular calcifications. We and Celgene are considering refocusing the sotatercept program on the treatment of patients with earlier, pre-dialysis kidney disease. We expect to meet with the FDA in the first half of 2016 to discuss the initiation of a clinical trial in pre-dialysis patients.

Sotatercept is also being studied through investigator-initiated clinical 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. Investigators at the University of Indiana initiated a Phase 2a clinical trial to evaluate the effects of sotatercept on bone mass and turnover 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 adult patients 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.

Dalantercept

Our third clinical stage therapeutic candidate, dalantercept, is designed to treat cancers by inhibiting blood vessel formation by inhibiting signaling through the ALK1 receptor. This mechanism is distinct from, and potentially synergistic with, the dominant class of cancer drugs that inhibit blood vessel formation, the vascular endothelial growth factor, or VEGF, pathway inhibitors. We are developing dalantercept primarily for use in combination with VEGF pathway inhibitors to produce better outcomes for cancer patients.

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), Cyramza® (ramucirumab), Inlyta® (axitinib), Nexavar® (sorafenib), Stivarga® (regorafenib), Sutent® (sunitinib), Votrient® (pazopanib), Caprelsa® (vandetanib), and Zaltrap® (ziv-aflibercept). Three large markets for which these drugs have been approved are non-small cell lung cancer, colorectal cancer and renal cell carcinoma.

Non-Small Cell Lung Cancer (NSCLC). The National Cancer Institute estimates there were 221,200 new cases of lung cancer in the United States in 2015 with 158,040 deaths. In 2015, sales of Avastin® in NSCLC were an estimated \$1.1 billion in the United States and \$1.8 billion worldwide.

Colorectal Cancer. The National Cancer Institute estimates there were 132,700 new cases of colon cancer or rectal cancer in the United States in 2015 with 49,700 deaths. In 2015, sales of Avastin® for colorectal cancer were an estimated \$1.3 billion in the United States and \$3.6 billion worldwide.

Renal Cell Carcinoma. The National Cancer Institute estimates there were 61,560 new cases of kidney and renal pelvis cancer in the United States in 2015 with 14,080 deaths. In 2015, U.S. sales of drugs for renal cell carcinoma were \$1.4 billion, of which \$1.0 billion were anti-angiogenesis drugs that target the VEGF pathway, principally

Table of Contents

Sutent®, Inlyta®, Votrient® and Avastin®. Worldwide sales in 2015 of drugs for renal cell carcinoma were \$3.5 billion, of which \$2.6 billion were drugs that target the VEGF pathway.

Other Tumors. One or more anti-angiogenesis agents are also approved as treatments for liver cancer, ovarian cancer, neuroendocrine tumors, soft tissue sarcoma, gastric cancer, thyroid cancer and glioblastoma.

We are evaluating dalantercept in combination with axitinib, a tyrosine kinase inhibitor of the VEGF pathway, for the treatment of renal cell carcinoma in the DART trial, a two part Phase 2 clinical trial. In Part 1 of the DART trial, dalantercept plus axitinib produced clinical outcomes that exceed historical results with axitinib alone. We have reported a median progression-free survival (PFS) for dalantercept plus axitinib of 8.3 months. There was no control arm in Part 1 of the DART trial, however published data from a prior phase 3 trial of axitinib alone (the AXIS trial) in a similar patient subgroup show a median PFS of 4.8 months. We are currently conducting Part 2 of the DART trial, which is a double-blind, placebo-controlled trial, in which an estimated 130 patients are randomized to dalantercept plus axitinib or placebo plus axitinib. We expect to report on progression free survival from Part 2 of the DART trial by the end of 2016. In the open-label Part 1 and blinded Part 2 of the DART trial, the following serious adverse events have been reported as related to dalantercept, dalantercept or placebo (blinded Part 2), or both dalantercept and axitinib: fluid overload, dyspnea, epistaxis, renal injury, acute renal failure and hyponatremia. Non-serious adverse events associated with axitinib did not generally occur with higher than expected frequency or severity. In addition to the DART trial, we are conducting a clinical trial to evaluate the treatment of patients with advanced hepatocellular cancer (HCC) with a combination of dalantercept plus sorafenib, another tyrosine kinase inhibitor of the VEGF pathway. A total of 21 patients have been enrolled as of December 30, 2015. The preliminary data indicate a general lack of efficacy for the dalantercept plus sorafenib combination in the treatment of advanced HCC, and therefore we believe that it is unlikely that additional patients will be enrolled in the HCC trial.

Dalantercept has been tested as a single-agent therapy in four completed clinical trials: a Phase 1 clinical trial and Phase 2 clinical trials in head and neck cancer, ovarian cancer and endometrial cancer. In these studies of dalantercept as monotherapy, there was not sufficient activity to warrant further development of dalantercept as monotherapy in these tumor types. We believe the greatest potential for dalantercept will be in combination with VEGF pathway inhibitors or in combination with cytotoxic chemotherapy.

ACE-083

Our fourth clinical stage therapeutic candidate, ACE-083, is designed to promote muscle growth and function in specific, targeted muscles. In 2014, we initiated a Phase 1 clinical trial with ACE-083 in healthy volunteers. ACE-083 has been well tolerated and no serious adverse events have been reported. Initial data from the Phase 1 trial showed that, at the highest dose level tested, ACE-083 generated a mean increase in muscle volume of approximately 14.5% in the treated muscle. We have completed enrollment for the ACE-083 Phase 1 clinical trial, and we expect to initiate a Phase 2 clinical trial with ACE-083 in patients with facioscapulohumeral dystrophy, or FSHD, in the second half of 2016.

FSHD is a severe, disabling, and painful skeletal muscle disease that presents with muscle-by-muscle progression. Muscle weakness can be heterogeneous, but is highly focal and primarily asymmetric. Typical onset occurs between the ages 20 and 40. Most FSHD patients live a normal lifespan, but many will suffer from disability, pain, and depression. FSHD is one of the most prevalent forms of muscular dystrophy affecting roughly 19,000 patients in the United States.

Preclinical Programs

In addition to our clinical development activities, we are expanding our research capabilities in order to increase the rate at which our highly productive research group can identify and advance new, internally discovered, therapeutic candidates for clinical development. Our discovery efforts are primarily focused on identifying new protein therapeutic candidates from our IntelliTrap™ platform and identifying novel antibodies. We have selected our first IntelliTrap™ therapeutic candidate, ACE-2494, for pre-clinical evaluation and advancement to clinical trials by the end of 2016. We are also evaluating ACE-3891 as a candidate therapeutic for the treatment of muscle disease, ACE-1332, a selective TGF-beta antagonist, for treatment of disorders with a fibrotic component, and ACE-2798, ACE-2536 and ACE-2395 for undisclosed therapeutic areas.

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 \$297.7 million from our collaborations with Celgene, Alkermes plc (Alkermes) and our terminated collaboration with Shire AG (Shire).

Table of Contents

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 luspatercept, which we refer to as the Luspatercept Agreement under which we granted to Celgene worldwide rights to luspatercept and also amended certain terms of the Sotatercept Agreement. These agreements provide Celgene exclusive licenses for these 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 December 31, 2015, we have received \$43.0 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 beta-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.

Luspatercept Agreement. Under the terms of the Luspatercept Agreement, we and Celgene are collaborating in the development and commercialization of luspatercept. 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 Luspatercept Agreement in August 2011 and, as of December 31, 2015, we have received \$60.3 million in research and development funding and milestone payments for the luspatercept 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 beta-thalassemia, as well as manufacturing the clinical supplies for these studies. Celgene will conduct subsequent Phase 2 and Phase 3 clinical trials. Acceleron will manufacture luspatercept for all Phase 1 and Phase 2 clinical trials, and Celgene will have responsibility for the manufacture of luspatercept 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 luspatercept program.

In November 2013, the Company has agreed to conduct additional development activities including clinical and non-clinical services, which are reimbursed under the same terms and rates of the existing Agreements. Please refer to Note 10 to the financial statements in this Annual Report on Form 10-K for the revenue recognition accounting, including changes in estimates, pursuant to the revenue recognition accounting literature.

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 Luspatercept 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, luspatercept 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 luspatercept. The royalty schedules for sotatercept and luspatercept are the same. Celgene is obligated to use commercially reasonable efforts to develop and commercialize sotatercept and luspatercept. Celgene may determine that it is commercially reasonable to develop and commercialize only luspatercept or sotatercept and discontinue the development or commercialization of the other therapeutic candidate, or Celgene may determine that it is not commercially reasonable to continue development of one or both of sotatercept and luspatercept. 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.

Table of Contents

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-beta 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 pursuing technology licensed under this collaboration. Rights pertaining to a lead program, referred to ACE-771, were returned pursuant to the terms of the agreement, and we are not pursuing development of ACE-771 at this point in time.

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 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 \$9.0 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 therapeutic candidates we may develop or 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 therapeutic candidates 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:

MDS

If either luspatercept or sotatercept 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 is currently studying erythropoiesis stimulating agent, Aranesp® and Janssen Pharmaceuticals is studying erythropoiesis stimulating agent Eprex