ACCELERON PHARMA INC
Form 10-K
February 27, 2019
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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549
FORM 10-K
(Mark One)

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

For the Fiscal Year Ended December 31, 2018

OR

o 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 Cambridge, Massachusetts (Address of principal executive offices)	02139 (Zip Code)

(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 ý No o
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 o No ý
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 ý No o
Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted 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 such files). Yes ý No o
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. ý

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

Large accelerated filer	ý	Accelerated filer	o
Non-accelerated filer	o	Smaller reporting company	o
		Emerging growth company	o

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. o

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

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 $1.6 billion.

As of January 31, 2019, the registrant had 51,690,462 shares of Common Stock, $0.001 par value per share, outstanding.

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DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive Proxy Statement relating to its 2019 Annual Meeting of Stockholders are incorporated by reference into Part III of this Annual Report on Form 10-K where indicated. Such Proxy Statement will be filed with the U.S. Securities and Exchange Commission within 120 days after the end of the fiscal year to which this report relates.

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FORWARD-LOOKING STATEMENTS

This Annual Report 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 ACE-083, ACE-2494 and our preclinical therapeutic candidates;
- 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 anticipated milestone payments under our collaboration agreements with Celgene;
- 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 manufacturing capabilities and strategy;
- our plans for commercialization and marketing;
- 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.

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PART I

Item 1. Business

We are a leading biopharmaceutical company in the discovery and development of TGF-beta superfamily therapeutics to treat serious and rare diseases. Our research focuses on key natural regulators of cellular growth and repair, particularly the Transforming Growth Factor-Beta, or TGF-beta, protein superfamily. 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 generated several innovative therapeutic candidates, all of which encompass novel potential first-in-class mechanisms of action. We have focused and prioritized our research and development activities within three key therapeutic areas: hematologic, neuromuscular and pulmonary. If successful, these candidates could have the potential to significantly improve clinical outcomes for patients across these areas of high, unmet need.

Luspatercept, our lead program, and sotatercept, are partnered with Celgene Corporation, or Celgene. Luspatercept is an investigational erythroid maturation agent designed to promote red blood cell production through a novel mechanism, and is being developed to treat chronic anemia and associated complications in myelodysplastic syndromes, or MDS, beta-thalassemia, and myelofibrosis. In 2018, we and Celgene announced positive results for two Phase 3 clinical trials with luspatercept; one for the treatment of patients with lower-risk MDS with ring sideroblasts, known as the MEDALIST trial, and another for the treatment of patients with transfusion-dependent beta-thalassemia, also known as the BELIEVE trial. In the MEDALIST trial, luspatercept achieved a highly statistically significant improvement in the primary endpoint of red blood cell (RBC) transfusion independence of at least 8 consecutive weeks during the first 24 weeks compared to placebo. In the BELIEVE trial, luspatercept achieved a highly statistically significant improvement in the primary endpoint of erythroid response, which was defined as at least a 33 percent reduction from baseline in red blood cell (RBC) transfusion burden with a reduction of at least 2 units during the protocol-defined period of 12 consecutive weeks, from week 13 to week 24, compared to placebo. Results from the MEDALIST and BELIEVE trials were then presented during plenary and oral sessions, respectively, at the 60th American Society of Hematology Annual Meeting and Exposition in December 2018, and we expect to submit these results for publication during 2019. Both of these presentations were selected for "Best of ASH," chosen from among the thousands of meeting abstracts as "the biggest breakthroughs from the meeting's scientific presentations." We and Celgene are planning regulatory application submissions for luspatercept in both MDS and beta-thalassemia in the United States in April 2019 and in Europe in the first half of 2019.

In addition to the MEDALIST and BELIEVE Phase 3 clinical trials with luspatercept, Celgene is currently conducting a Phase 2 clinical trial in non-transfusion-dependent beta-thalassemia patients, referred to as the BEYOND trial, with preliminary top-line results currently expected in 2020. Celgene has also initiated a Phase 3 clinical trial, the COMMANDS trial, in first-line, lower-risk MDS patients and enrollment is ongoing. Enrollment is also currently ongoing in a Phase 2 clinical trial being conducted by Celgene for the treatment of patients with myelofibrosis, a rare bone marrow disorder, with preliminary top-line results currently expected in the second half of 2019. If luspatercept were to receive regulatory approval for each of these indications in the United States and Europe, we believe that there is an annual peak sales opportunity for luspatercept in excess of $2 billion across the indications in the BEYOND trial and the luspatercept Phase 3 clinical trials, and an annual peak sales opportunity for luspatercept in excess of $1 billion in myelofibrosis. We and Celgene are also evaluating further research of luspatercept for the treatment of anemia in potential new indications that could provide additional sales opportunities.

For sotatercept, we have the rights to fund, develop, and lead the global commercialization of sotatercept in pulmonary hypertension, which we refer to as the PH field, including pulmonary arterial hypertension, or PAH. PAH is a rare and chronic, rapidly progressing disorder characterized by the constriction of small pulmonary arteries, resulting in abnormally high blood pressure in the pulmonary arteries. We are currently enrolling the PULSAR Phase 2 clinical trial of sotatercept for the treatment of patients with PAH with preliminary results expected in the first half of 2020, and we recently initiated an exploratory study, called SPECTRA, in the first quarter of 2019 to provide us with further understanding of sotatercept's impact on PAH. If sotatercept is commercialized to treat PAH and we recognize such revenue, then Celgene will be eligible to receive a royalty in the low 20% range on global net sales. In certain circumstances Celgene may recognize revenue related to the commercialization of sotatercept in PAH, and in

this scenario we will be eligible to receive a royalty from Celgene such that the economic position of the parties is equivalent to the scenario in which we recognize such revenue.

For luspatercept and, outside of the PH field, sotatercept, Celgene is responsible for paying 100% of the development costs for all clinical trials. We may receive a maximum of $545.0 million for the potential development, regulatory and commercial milestone payments. If luspatercept and, outside of the PH field, sotatercept are commercialized, we are eligible to receive a royalty on net sales in the low-to-mid 20% range. We have a co-promotion right in North America, for which our commercialization costs provided in the commercialization plan and budget as approved by the Joint Commercialization Committee will be entirely funded by Celgene, and from time to time we may elect to conduct additional activities to support commercialization of luspatercept at our own expense.

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We are independently developing our wholly-owned neuromuscular candidate, ACE-083. ACE-083 is designed for the treatment of focal muscle disorders, and we are currently conducting Phase 2 clinical trials with ACE-083 in patients with facioscapulohumeral muscular dystrophy, or FSHD, as well as in patients with Charcot-Marie-Tooth disease, or CMT. We previously announced results from part 1 of each of our Phase 2 clinical trials in patients with FSHD and CMT showing increases in mean total and contractile muscle volume, reductions in fat fraction, and an encouraging safety profile. Enrollment is complete in part 2 of the ACE-083 Phase 2 clinical trial in patients with FSHD and is ongoing in the ACE-083 Phase 2 clinical trial in patients with CMT. We expect to announce preliminary results from part 2 of each of these Phase 2 clinical trials by the second half of 2019 for FSHD and by year end for CMT.

In addition to our mid- to late-stage clinical programs, we are currently conducting a Phase 1 healthy volunteer study with ACE-2494, our wholly-owned systemic muscle agent from our proprietary platform technology, IntelliTrap™, and we expect to report preliminary results from this healthy volunteer study in the first half of 2019. We are also conducting research primarily within our three focused disease areas—hematologic, neuromuscular and pulmonary—in order to identify new therapeutic candidates to advance into clinical trials.

As of December 31, 2018 our operations have been funded primarily by $105.1 million in equity investments from venture investors, $539.7 million from public investors, $123.7 million in equity investments from our collaboration partners and $284.2 million in upfront payments, milestones, and net research and development payments from our collaboration partners. In addition, we raised an additional $248.2 million in net proceeds in connection with our offering of 6,151,163 shares of our common stock in January 2019.

Our Goals and Objectives in the Year 2019

By building on the milestones achieved in 2018, we intend to advance and expand our pipeline in 2019 and prepare for the potential commercialization of luspatercept, and we plan to achieve the following goals and objectives:

Hematology

- Luspatercept

Myelodysplastic syndromes (MDS), beta-thalassemia and myelofibrosis:

Marketing authorization applications for lower-risk MDS and beta-thalassemia in the U.S. in April 2019 and in the E.U. the first half of 2019

MEDALIST and BELIEVE Phase 3 trial results submitted for publication

Expansion of clinical program into other indications

Continue enrollment of BEYOND Phase 2 trial

Continue enrollment of COMMANDS Phase 3 trial

Announce preliminary results from the Phase 2 trial in patients with anemia associated with myelofibrosis in the second half of 2019

Neuromuscular

- ACE-083

Announce preliminary results for Part 2 of the Phase 2 clinical trial of ACE-083 in patients with FSHD in the second half of 2019

Announce preliminary results for Part 2 of the Phase 2 clinical trial of ACE-083 in patients with CMT by year end

- ACE-2494

Announce preliminary results for the Phase 1 healthy volunteer clinical trial with ACE-2494

Pulmonary

- Sotatercept

Initiate SPECTRA exploratory study in the first quarter of 2019

Fully enroll PULSAR Phase 2 clinical trial by year end

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

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gene expression that guide cell growth and differentiation. The TGF-beta superfamily ligands and their receptors represent a diverse 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 multiple Fc-fusion protein ligand traps, our novel IntelliTrap™ platform technology and a robust pipeline of innovative clinical and preclinical therapeutic candidates targeting key mechanisms underlying serious 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. This collaboration could expand our biologics platform and provide us with enhanced access to antibody therapeutic candidates in the future.

We use our integrated platform of research, development and manufacturing technologies to rapidly and cost-effectively create, test and advance our therapeutic candidates. Our leadership in the understanding of TGF-beta biology and protein engineering generates innovative compounds that engage the body's ability to regulate cellular growth and repair.

Our Pipeline

Luspatercept

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

Myelodysplastic Syndromes (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 over 15,000 cases and the overall U.S./EU prevalence at least 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 75% of the MDS patients in the U.S. and

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EU are classified as lower risk and 25% 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. Many categorized as lower-risk typically receive ESAs as first-line therapy, though ESAs are not approved by the FDA for the treatment of anemia in MDS patients. Therapeutic options following failure on ESAs are limited, and most patients end up receiving red blood cell transfusions to manage their anemia. Approximately 15% of patients with MDS have a specific chromosomal mutation and are treated with Revlimid®.

The chronic 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 chronic 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 inhibits red blood cell maturation. For this reason, we believe that blocking this excess signaling by luspatercept may reverse this inhibition. More than half 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 chronic anemia resulting from ineffective erythropoiesis is a major cause of morbidity in MDS patients.

MEDALIST

In December 2018, we and Celgene announced results from the pivotal, phase 3 MEDALIST trial with luspatercept, and the MEDALIST data were presented by Alan F. List, M.D. of the Moffitt Cancer Center during the Plenary Scientific Session at the 60th American Society of Hematology (ASH) Annual Meeting and Exposition. MEDALIST is a phase 3, randomized, double blind, placebo-controlled, multi-center study evaluating the safety and efficacy of luspatercept in patients with very low-, low-, or intermediate-risk non-del(5q) MDS. All patients were RBC transfusion dependent and were either refractory or intolerant to prior erythropoiesis-stimulating agent (ESA) therapy, or were ESA naïve with endogenous serum erythropoietin ≥ 200 U/L, and had no prior treatment with disease modifying agents. The median age of the patients enrolled in the trial was 71 years in the luspatercept treatment group and 72 years in the placebo group. Median transfusion burden in both treatment arms was 5 RBC units/8 weeks. 229 patients were randomized to receive either luspatercept 1.0 mg/kg (153 patients) or placebo (76 patients) via subcutaneous injection once every 21 days. The study was conducted at 65 sites in 11 countries.

MEDALIST met the primary endpoint of red blood cell transfusion independence (RBC-TI) for 8 or more weeks during the first 24 weeks of the study. Treatment with luspatercept resulted in a statistically significantly greater proportion of patients achieving RBC-TI ≥ 8 weeks compared to placebo. The study also found in secondary endpoints that treatment with luspatercept resulted in a statistically significant higher percentage of patients achieving RBC-TI of 12 or more weeks in the first 24 or 48 weeks of the study, as well as hematologic improvement-erythroid (HI-E) of 8 or more weeks.

Endpoints	Luspatercept	Placebo	P-Value
RBC-TI ≥8 weeks (weeks 1-24)	37.9% (58/153)	13.2% (10/76)	< 0.0001
RBC-TI ≥12 weeks (weeks 1-24)	28.1% (43/153)	7.9% (6/76)	0.0002
RBC-TI ≥12 weeks (weeks 1-48)	33.3% (51/153)	11.8% (9/76)	0.0003
HI-E ≥ 8 weeks (IWG 2006, weeks 1-24)	52.9% (81/153)	11.8% (9/76)	< 0.0001

MEDALIST Safety Summary

Treatment-emergent adverse events (TEAEs) of Grade 3 or 4 were reported in 42.5% (65/153) of patients receiving luspatercept and 44.7% (34/76) of patients receiving placebo. Progression to acute myeloid leukemia (AML) occurred in four patients, three patients (2.0%) receiving luspatercept and one patient (1.3%) receiving placebo. Five patients receiving luspatercept (3.3%) and four patients receiving placebo (5.3%) experienced one or more TEAE that resulted in death.

Most common TEAEs of any Grade in Greater than 10% of Patients in Either Arm

	Luspatercept N=153	Placebo N=76
Fatigue	26.8%	13.2%
Diarrhea	22.2%	9.2%
Asthenia	20.3%	11.8%

Nausea	20.3%	7.9%
Dizziness	19.6%	5.3%
Back pain	19.0%	6.6%

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Luspatercept is not approved in any region for any indication. We and Celgene are planning regulatory application submissions of luspatercept in the United States in April 2019 and in Europe in the first half of 2019.

COMMANDS

Celgene is also currently conducting the COMMANDS Phase 3 trial in first-line, lower-risk MDS patients and enrollment is ongoing.

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.

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 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, respectively.

Beta-thalassemia is particularly prevalent throughout the Mediterranean region, Middle East, and Southeast Asia, and, due to migration and immigration, is increasingly 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 $80,000 per year in the United States and certain countries in Europe 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.

Although no drug is currently approved to treat the anemia of beta-thalassemia, hematopoietic stem cell transplantation is used as a potentially curative approach for beta-thalassemia, however 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. Bluebird bio’s gene therapy program, LentiGlobin®, a gene-therapy program delivered after single-agent, myeloablative busulfan conditioning, was granted accelerated assessment by the European Medicines Agency for patients with transfusion dependent beta-thalassemia in the fourth quarter of 2018 and may submit a Biologics License Application to FDA by the end of 2019.

BELIEVE

In December 2018, we and Celgene also announced results from the pivotal, phase 3 BELIEVE trial with luspatercept, and the BELIEVE data were presented by Maria Domenica Cappellini, M.D. in an oral session at the 60th ASH Annual Meeting and Exposition. BELIEVE is a phase 3, randomized, double blind, placebo-controlled multicenter study comparing luspatercept + best supportive care (BSC) versus placebo + BSC in adult beta-thalassemia patients who require regular RBC transfusions. The median age of the patients was 30 years in both treatment arms. 336 patients were randomized 2:1 to receive either luspatercept 1.0 mg/kg + BSC (224 patients) or placebo + BSC (112 patients) every 3 weeks for up to 48 weeks. Patients in the luspatercept + BSC arm were able to be titrated up to 1.25 mg/kg of luspatercept every 3 weeks. BSC was defined as RBC transfusions and iron chelation therapy to maintain each patient’s baseline hemoglobin level. Crossover to the luspatercept treatment group was allowed after unblinding and assessment by an independent Data Safety Monitoring committee; patients receiving luspatercept + BSC will be followed for up to 3 years. The study was conducted at 65 sites in 15 countries.

BELIEVE met the primary endpoint of erythroid response, defined as a ≥33% reduction in RBC transfusion burden (with a reduction of ≥ 2 units of RBC) during weeks 13-24 compared to the baseline 12-week interval prior to

randomization. The study also included secondary endpoints that evaluated the impact of treatment on RBC transfusion burden. Mean change in transfusion burden from baseline to weeks 13-24 (luspatercept vs. placebo) was -1.35 RBC units.

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RBC Transfusion Burden Reduction of ≥ 33% Response Rates[1]

Response Time Interval	Luspatercept	Placebo	P-value
Weeks 13-24	21.4% (48/224)	4.5% (5/112)	< 0.0001
Weeks 37-48	19.6% (44/224)	3.6% (4/112)	< 0.0001
Any 12 weeks during the entire treatment period	70.5% (158/224)	29.5% (33/112)	< 0.0001
Any 24 weeks during the entire treatment period	41.1% (92/224)	2.7% (3/112)	< 0.0001

[1]RBC transfusion burden reduction response rates are calculated versus baseline (i.e., the 12 weeks prior to randomization)

RBC Transfusion Burden Reduction of ≥ 50% Response Rates[1]

Response Time Interval	Luspatercept	Placebo	P-value
Weeks 13-24	7.6% (17/224)	1.8% (2/112)	0.0303
Weeks 37-48	10.3% (23/224)	0.9% (1/112)	0.0017
Any 12 weeks during the entire treatment period	40.2% (90/224)	6.3% (7/112)	< 0.0001
Any 24 weeks during the entire treatment period	16.5% (37/224)	0.9% (1/112)	< 0.0001

[1]RBC transfusion burden reduction response rates are calculated versus baseline (i.e., the 12 weeks prior to randomization)

BELIEVE Safety Summary (Safety Population)

Grade 3 or higher treatment-emergent adverse events (TEAEs) were reported in 29.1% (65/223) of patients receiving luspatercept and 15.6% (17/109) of patients receiving placebo. Serious adverse events were reported in 15.2% (34/223) of patients receiving luspatercept and 5.5% (6/109) of patients receiving placebo. A TEAE of acute cholecystitis resulted in death in one placebo-treated patient (0.9%). No luspatercept-treated patients died due to TEAEs.

Grade 3 or 4 TEAEs in at least 1% of patients in either arm

	Luspatercept N= 223	Placebo N= 109
Anemia	3.1%	0.0%
Increased liver iron concentration	2.7%	0.9%
Hyperuricemia	2.7%	0.0%
Hypertension	1.8%	0.0%
Syncope	1.8%	0.0%
Back pain	1.3%	0.9%
Bone pain	1.3%	0.0%
Blood uric acid increased	1.3%	0.0%
Increased aspartate aminotransferase	1.3%	0.0%
Increase alanine aminotransferase	0.9%	2.8%
Thromboembolic events*	0.9%	0.0%

*All grades of thromboembolic events, including DVT, PE, portal vein thrombosis, ischemic stroke, thrombophlebitis, and superficial phlebitis were reported in 8 of 223 (3.6%) luspatercept-treated versus 1 of 109 (0.9%) placebo-treated patients

BEYOND

Celgene is also currently conducting a Phase 2 clinical trial in non-transfusion-dependent beta-thalassemia patients, referred to as the BEYOND trial, with preliminary top-line results currently expected in 2020.

Myelofibrosis

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. Epidemiological databases suggest that there are approximately 30,000 myelofibrosis patients in the United States and Europe. Approximately 30% of myelofibrosis patients present primarily with anemia when diagnosed and

nearly all patients will develop anemia with progression of the disease. There is no approved drug therapy to treat chronic anemia in myelofibrosis. Our and Celgene's objective is to develop luspatercept as a treatment for the chronic anemia in myelofibrosis patients, and

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Celgene has initiated a Phase 2 clinical trial in patients with myelofibrosis and enrollment is ongoing, with preliminary top-line results currently expected in the second half of 2019.

Sotatercept

Sotatercept is an activin receptor type IIA fusion protein that acts as a ligand trap for members in the TGF-beta protein superfamily involved in the remodeling of a variety of different tissues, including the vasculature and fibrotic tissue. In Phase 1 and Phase 2 clinical trials involving approximately 400 patients, sotatercept has been shown in humans to promote the formation of red blood cells, increase bone mineral density and reduce calcified blockages in the vasculature (vascular calcification). We have recently discovered that sotatercept has a potent effect in improving cardiovascular health in mouse models of a disease termed pulmonary arterial hypertension, or PAH.

Pulmonary Arterial Hypertension (PAH)

Pulmonary hypertension is a group of diseases characterized by elevated blood pressure in the pulmonary circulation resulting from a variety of causes. PAH is a type of pulmonary hypertension. It is a rare, chronic, rapidly progressing disorder characterized by the constriction of small pulmonary arteries, resulting in abnormally high blood pressure in these vessels. Patients typically present with exercise fatigue and shortness of breath. Progressive obstruction and constriction of the pulmonary vasculature leads to elevated blood pressure in the pulmonary circulation and strain on the right side of the heart. In later stages of disease, right heart failure may develop, and heart failure is the major cause of death in PAH patients. The major classes of drugs used to treat PAH are: the phosphodiesterase 5 inhibitors (PDE5i), the endothelin receptor antagonists (ERAs), the soluble guanylate cyclase stimulators (sGCs) and the prostacyclins. Despite the availability of therapeutic options, the disease progresses rapidly and the five-year survival rate for patients is approximately 57%. All classes of currently approved therapies are designed to promote the dilation of blood vessels, a mechanism referred to as vasodilation. As evident from the high mortality rate, therapies that promote vasodilation improve many aspects of the disease, but do not fundamentally modify or halt the progression of the disease. Accordingly, there is significant unmet need for therapies that address more fundamental aspects of the disease.

Heritable forms of PAH are known, and the underlying genetic defects have been identified. In most cases, the underlying mutations map to a gene that encodes the BMP receptor type II (BMPRII) or genes encoding other proteins that participate in the BMPRII signaling pathway. BMPRII is a key receptor for ligands referred to as the BMPs, and these are part of the TGF-beta superfamily. The BMP-BMPRII signaling pathway activates transcription factors called Smad1/5/8 that coordinate changes in the expression of certain genes. A deficiency in BMP-BMPRII signaling, and the attendant activation of Smad1/5/8, is thought to lead to increased proliferation of cell types that line the vessels, including endothelial cells, smooth muscle cells and fibroblasts. This increased proliferation leads to an overgrowth of smooth muscle and fibrotic tissue around the small arterioles, leading to the formation of muscularized vessels and so-called plexiform lesions. The vessels become constricted and obstructed. Plexiform lesions are arterioles that have become almost completely obstructed by an over-proliferation of endothelial cells, smooth muscle cells and fibrotic tissue. Although the association between BMP-BMPRII signaling and PAH was first identified through the study of patients with heritable forms of the disease, it is now understood that BMP-BMPRII signaling is deficient in patients with non-heritable forms of the disease, including idiopathic and associated forms of PAH. For these reasons, it is expected that a therapeutic agent that improves the signaling deficits in the BMP-BMPRII pathway, activating Smad1/5/8, could rectify key defective molecular signaling events causing the disease, with the potential to modify the course of disease.

It has been reported that a group of proteins targeted by sotatercept, the activins, are present at increased levels in PAH patients. Recently, we and others have found that activins can suppress signaling through the BMP-BMPRII pathway, as measured by assessing Smad1/5/8 activation. We further found that sotatercept, by inhibiting activins, can stimulate the BMP-BMPRII signaling pathway in isolated cells. We evaluated sotatercept for its effects on the establishment of PAH in two mouse models of the disease, and we found that sotatercept had a more profound benefit than representatives of any of the classes of standard-of-care therapies. As a result, we believe that sotatercept has the potential to correct the BMP-BMPRII signaling deficit that is fundamental to disease in PAH patients and thereby modify the course of disease. Further, because sotatercept works by a distinct mechanism from the available vasodilator agents, we believe that sotatercept can be used in combination with these other agents.

The worldwide PAH patient population is expanding, with more than 80,000 patients living with PAH in the United States and European Union combined. PAH represents one of the largest specialty pharmaceutical markets with more than $3.7 billion in sales in the United States in 2017.

PULSAR and SPECTRA

In May 2018, we initiated the PULSAR Phase 2 clinical trial with sotatercept, or the PULSAR trial. The PULSAR trial is a randomized, double-blind, placebo-controlled study designed to evaluate the efficacy and safety of sotatercept in PAH

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patients. The primary endpoint of the PULSAR trial is the change from baseline in pulmonary vascular resistance (PVR) over a 24-week treatment period. The key secondary endpoint is change from baseline in six-minute walk distance (6MWD). A total of 100 patients will be randomized 3:3:4 into three treatment arms with standard-of-care vasodilator therapies in combination with sotatercept or placebo. Following the 6-month double-blind treatment period, participants in the trial will be eligible to enroll into the 18-month extension period. Enrollment is currently ongoing in the PULSAR trial and we expect to announce preliminary results in the first half of 2020.

We also recently announced that we initiated the SPECTRA exploratory study with sotatercept in the first quarter of 2019 to provide us with further understanding of sotatercept's impact on PAH.

ACE-083

Our third clinical stage therapeutic candidate, ACE-083, is designed to promote muscle growth and function in specific, targeted muscles. ACE-083 uses the Myostatin + approach to promote muscle growth, meaning that ACE-083 inhibits myostatin, a well-characterized regulator of muscle size, as well as other factors that suppress muscle growth. Through the inhibition of multiple suppressors of muscle growth, ACE-083 promotes a substantially greater muscle mass increase than selective myostatin antagonists. We are currently conducting Phase 2 clinical trials with ACE-083 in patients with facioscapulohumeral dystrophy, or FSHD, as well as in patients with Charcot-Marie-Tooth disease, or CMT.

FSHD

FSHD is a severe, disabling, and painful skeletal muscle disease that presents with muscle-by-muscle progression. Muscle weakness is highly focal and often asymmetric, and frequently includes lower leg weakness resulting in foot drop and upper arm weakness. 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. Current treatment is largely limited to orthotic or surgical intervention to provide or maintain functionality. FSHD is one of the most prevalent forms of muscular dystrophy affecting roughly 20,000 patients in the United States.

In 2018, we announced preliminary results for part 1 of the Phase 2 clinical trial with ACE-083 in patients with FSHD. These preliminary results included data from 36 patients evaluable for magnetic resonance imaging, or MRI, among six different cohorts with all patients open-label receiving ACE-083 as a unilateral or bilateral intramuscular injection once every three weeks for 12 weeks. The cohorts consisted of 12 patients with tibialis anterior weakness treated unilaterally with either 150mg/muscle (6 patients) or 200mg/muscle (6 patients), 6 patients with tibialis anterior weakness treated bilaterally with 200mg/muscle, and 18 patients with biceps brachii weakness treated unilaterally with 150mg, 200mg, or 240mg/muscle (6 patients each). Mean total muscle volume increases (plus or minus standard error mean, or ± SEM) and mean decreases (± SEM), or improvements, in fat fraction percentage relative to baseline were measured by MRI at 3 weeks after the last dose of ACE-083, and were as follows:

Muscle	ACE-083 Dose/Muscle	Number of Patients	Total Muscle Volume Increase (percent change) (mean ± SEM)	Decrease in Fat Fraction, % (absolute change) (mean ± SEM)
Tibialis Anterior	150mg unilateral	6	8.1 (3.5)	-4.5 (3.0)[1]
Tibialis Anterior	200mg unilateral	6	16.8 (3.0)	-5.0 (2.8)
Tibialis Anterior	200mg bilateral	6	18.8 (3.1)	-5.7 (0.8)
Biceps Brachii	150mg unilateral	6	8.2 (6.0)	-1.2 (1.3)
Biceps Brachii	200mg unilateral	6	17.1 (7.8)	-0.1 (1.3)
Biceps Brachii	240mg unilateral	6	16.2 (4.7)	0.6 (0.9)

[1]N=5 patients. Data for one patient was not available.

ACE-083 was well tolerated in part 1 of the FSHD Phase 2 clinical trial and no study-drug related serious adverse events were reported. The most common adverse events were injection site reactions and myalgia and were grades 1-2. One patient experienced a related grade 3 non-serious adverse event of lower leg intramuscular swelling. This patient fully recovered and was discontinued from the study. We expect to announce preliminary results from the randomized, double blind, placebo-controlled part 2 of the FSHD Phase 2 clinical trial by the second half of this year.

CMT

CMT is one of the most common inherited neurologic diseases estimated to affect more than 125,000 people in the United States. The primary clinical manifestations of CMT include muscle weakness in the lower legs and hands. The lower leg

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muscle weakness can result in foot drop and a high-stepped gait leading to frequent tripping or falls. The disease is typically diagnosed by the presence of a characteristic pattern of muscle weakness, neurologic symptoms, and family history, as well as through genetic testing.

In 2018, we announced preliminary results for part 1 of the Phase 2 clinical trial with ACE-083 in patients with CMT. These preliminary results included data from 18 patients evaluable for magnetic resonance imaging, or MRI, among three different cohorts with patients receiving ACE-083 as a bilateral injection into the tibialis anterior muscle once every three weeks for 12 weeks. The cohorts consisted of 18 patients with tibialis anterior weakness treated bilaterally with 150mg, 200mg or 240mg/muscle (6 patients each). Mean total muscle volume increases (plus or minus standard error mean, or ± SEM) and mean decreases (± SEM), or improvements, in fat fraction percentage relative to baseline were measured by MRI at 3 weeks after the last dose of ACE-083, and were as follows:

Muscle	ACE-083 Dose/Muscle	Number of Patients	Total Muscle Volume Increase (percent change) (mean ± SEM)	Decrease in Fat Fraction, % (absolute change) (mean ± SEM)
Tibialis Anterior	150mg bilateral	6	12.6 (2.9)	-1.7 (1.2)
Tibialis Anterior	200mg bilateral	6	13.3 (1.5)	-3.5 (1.0)
Tibialis Anterior	240mg bilateral	6	14.2 (3.2)	-3.3 (1.2)

ACE-083 was well tolerated in part 1 of the CMT Phase 2 clinical trial and no study-drug related serious adverse events were reported. The most common adverse events were injection site reactions, muscle spasms and myalgia and were grades 1-2. We expect to announce preliminary results from the randomized, double blind, placebo-controlled part 2 of the CMT Phase 2 clinical trial by the end of this year.

ACE-2494

In addition to our mid- to late-stage clinical programs, we are currently conducting a Phase 1 healthy volunteer study with ACE-2494, our wholly-owned systemic muscle agent from our proprietary platform technology, IntelliTrap™, and we expect to report initial results from this healthy volunteer study in the first half of 2019.

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 fusion protein platform, which includes the IntelliTrap™ platform, and identifying novel antibodies. We are currently evaluating ACE-1334, a selective TGF-beta antagonist, for treatment of disorders with a fibrotic component, and additional molecules from our IntelliTrap™ platform 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 $408.0 million from our collaborations with Celgene and our prior collaborations with Alkermes plc (Alkermes) and Shire AG (Shire).

Celgene

On February 20, 2008 we entered into an agreement with Celgene relating to sotatercept, which we refer to as the Original Sotatercept Agreement. We amended the Original Sotatercept Agreement on August 2, 2011, which we refer to as the Amended Sotatercept Agreement. We further amended and restated the Amended Sotatercept Agreement in its entirety on September 18, 2017, and refer to the amended and restated agreement as the Restated Sotatercept Agreement. On August 2, 2011 we entered into a second agreement with Celgene for luspatercept, which we refer to as the Luspatercept Agreement.

Restated Sotatercept Agreement. The Restated Sotatercept Agreement provides Celgene with an exclusive license to sotatercept outside of the field of pulmonary hypertension, referred to as the PH field, and provides us with the worldwide rights to develop and commercialize sotatercept in the PH field. 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 Original Sotatercept Agreement and, as of December 31, 2018, we have received $44.5 million in research and development funding and milestone payments for the sotatercept program.

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In connection with the Restated Sotatercept Agreement, Celgene agreed not to develop or commercialize in the PH field any compound developed under the Restated Sotatercept Agreement or the Luspatercept Agreement, and we agreed not to develop or commercialize any compound developed under the Restated Sotatercept Agreement or the Luspatercept Agreement in any field outside of the PH field. We have the right to license, transfer or sell our rights to develop and commercialize sotatercept in the PH field, subject to Celgene's right of first negotiation.

We are responsible for 100% of the costs related to our development and commercialization of sotatercept in the PH field. If sotatercept is commercialized in the PH field and we recognize such revenue, then Celgene will be eligible to receive a royalty in the low 20% range on global net sales. In certain circumstances Celgene may recognize revenue related to the commercialization of sotatercept in the PH field, and in this scenario, we will be eligible to receive a royalty from Celgene such that the economic position of the parties is equivalent to the scenario in which we recognize such revenue. With respect to the development and commercialization of sotatercept outside of the PH field or the development and commercialization of any other compound under the Restated Sotatercept Agreement, the terms of the Amended Sotatercept Agreement remained unchanged.

Since January 1, 2013, Celgene has been responsible for paying 100% of worldwide development costs for the sotatercept program outside of the PH field and Celgene will be responsible for all commercialization costs worldwide, as approved in budgets agreed to between us and Celgene. We will be eligible to receive tiered royalty payments in the low-to-mid 20% range on net sales of sotatercept outside of the PH field. We are obligated to co-promote sotatercept outside of the PH field and future products in all fields, in each case if approved, in North America, and Celgene will pay all costs related thereto pursuant to the commercialization plan and budget. Outside the PH field, Celgene will be responsible for any sotatercept Phase 3 clinical trials, as well as any additional Phase 2 clinical trials, and is responsible for manufacturing or overseeing the manufacture of Phase 3 and commercial supplies.

Pursuant to the Restated Sotatercept Agreement, Celgene will provide us with certain quantities of Celgene's existing clinical supply of sotatercept for development in the PH field at no cost to us. For clinical supply of sotatercept in excess of that which is agreed to under the Restated Sotatercept Agreement, Celgene had the option to provide us with such clinical supply of sotatercept, but has declined this option, and we will be responsible for manufacturing future clinical supply of sotatercept in the PH field. Celgene may elect, however, to provide us with commercial supply of sotatercept at a negotiated price or provide a tech transfer to us to enable us to manufacture on our own behalf. The conduct of the collaboration is managed by a Joint Development Committee and Joint Commercialization Committee. In the event of a deadlock of a committee, we shall determine the resolution of issues specifically related to the PH field (other than pricing which shall be determined by consensus), and Celgene shall determine the resolution of all other issues. The Joint Commercialization Committee will oversee commercialization of sotatercept and sotatercept pricing will be determined by mutual agreement of us and Celgene in the Joint Commercialization Committee.

The Restated Sotatercept Agreement will expire on a country-by-country basis on the occurrence of the latest to occur of the following: (1) the expiration of the royalty term with respect to all license products outside the PH field in such country, (2) the expiration of the royalty term with respect to all sotatercept licensed products in the PH field in such country, and (3) the exercise or forfeiture by Celgene of its option with regard to each option compound. In the PH field, the royalty term for each licensed product in each country is the period commencing with first commercial sale of the applicable licensed product in the applicable country and ending on the latest of expiration of specified patent coverage or a specified period of years. Outside the PH field, the royalty term for each licensed product in each country outside North America is the period commencing with first commercial sale of the applicable licensed product in the applicable country and ending on the latest of expiration of specified patent coverage or a specified period of years, and the royalty term for each licensed product in North America is the period commencing with the first commercial sale in North America and ending, on a licensed product and country-by-country basis on the date which commercialization of such licensed product has ceased. The term for each option compound runs for a specified period of years unless Celgene exercises its option, in which case the compound becomes a licensed product, or forfeits its option by failing to make certain payments following the achievement of certain milestones in early clinical development of the option compound.

The Restated Sotatercept Agreement is 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 Restated Sotatercept 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 to Celgene and the rights granted to us with respect to the development of sotatercept in the PH field shall become irrevocable. Termination for cause by either party shall result in reducing the remaining royalties due to the breaching party by a certain percentage. Upon termination by Celgene for convenience or for failure to meet an endpoint, we and Celgene will enter into a termination agreement pursuant to which, among other things, Celgene will continue to be eligible to receive a royalty in the low 20% range on global net sales of sotatercept in the PH field.

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We are eligible to receive future development, regulatory and commercial milestones of up to $360.0 million for the sotatercept program outside of the PH field 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. We were not required to make any upfront payments to Celgene upon execution of the Restated Sotatercept Agreement, and we will not be required to make any milestone payments to Celgene in connection with our development and commercialization of sotatercept in the PH field.

Luspatercept Agreement. The Luspatercept Agreement provides Celgene with an exclusive license to luspatercept in all indications and 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, 2018, we have received $109.6 million in research and development funding and milestone payments for the luspatercept program.

Under the Luspatercept 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. Since January 1, 2013, Celgene has been responsible for paying 100% of worldwide development costs for the luspatercept program and Celgene will be responsible for all commercialization costs worldwide, as approved in the budgets agreed to between us and Celgene. We are obligated to co-promote luspatercept and future products, in each case if approved, in North America, and Celgene will pay all costs related thereto. From time to time we may elect to conduct additional activities to support luspatercept at our own expense. We will be eligible to receive tiered royalty payments in the low-to-mid 20% range on net sales of luspatercept. The Luspatercept Agreement is 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 Luspatercept 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.

Under the Luspatercept 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 may supply additional clinical supplies for our ongoing Phase 2 clinical trials in MDS and beta-thalassemia if needed. Celgene will conduct any subsequent Phase 2 and Phase 3 clinical trials. We were responsible for manufacturing luspatercept for all Phase 1 and Phase 2 clinical trials, and Celgene has responsibility for the manufacture of luspatercept for any additional Phase 2 and Phase 3 clinical trials and commercial supplies. We are eligible to receive future development, regulatory and commercial milestones of up to $185.0 million for the luspatercept program.

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 luspatercept 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 in the United States, current practice guidelines include the use of erythropoiesis stimulating agents and granulocyte colony stimulating factor agents (G-CSF) to treat patients with MDS. Eprex® from Janssen Pharmaceuticals was recently approved in Europe to treat symptomatic anemia in certain patients with lower risk MDS.

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- Red blood cell transfusions, which are used to treat anemia in patients with MDS, and iron chelation therapy, such as Novartis's oral iron chelating agents Exjade® and Jadenu™, which are used to treat iron overload in patients with MDS.
- Immunomodulators, including Celgene's approved product, Revlimid® (lenalidomide), for the treatment of anemia of certain MDS patients.
- Fibrogen is studying roxadustat (FG-4592), a hypoxia-inducible factor prolyl hydroxylase inhibitor in a Phase 3 study in lower risk MDS patients with anemia and low transfusion burden.
- 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 clinical trials in the United States and Europe; an anti-cancer therapy being developed by Onconova to treat patients with MDS; a telemorase inhibitor, imetelstat, being studied by Geron and Janssen in a Phase 2/3 study in lower risk MDS patients; and a CD95 ligand inhibitor, APG101, being studied by Apogenix, completed a Phase 1 study in transfusion dependent, lower risk MDS patients.

Beta-thalassemia

If luspatercept is approved for the treatment of patients with beta-thalassemia, it would compete with:

- Red blood cell transfusions, which are used to treat anemia in patients with beta-thalessemia, and iron chelation therapy, such as Novartis's oral iron chelating agents Exjade® and Jadenu™, which are used to treat iron overload in patients with beta-thalessemia.
- 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 beta-thalassemia.
- Hematopoietic stem cell transplant treatment is given to a small percentage of patients with beta-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.
- Bluebird bio’s gene therapy program, LentiGlobin®, was granted accelerated assessment by the European Medicines Agency for patients with transfusion dependent beta-thalassemia in the fourth quarter of 2018 and may submit a Biologics License Application to FDA by the end of 2019.
- Other therapies in development, including gene therapy and genome editing are being developed by several different groups, including GlaxoSmithKline plc, Sangamo BioSciences Inc. in collaboration with Bioverativ, and CRISPR Therapeutics in collaboration with Vertex.

Myelofibrosis

If luspatercept is approved for the treatment of patients with myelofibrosis, it would compete with:

- Recombinant erythropoietin, other erythropoiesis stimulating agents and immunomodulatory drugs. Although these agents are not approved to treat anemia in myelofibrosis in the United States, current practice guidelines include the use of these agents to treat anemia in patients with myelofibrosis.
- A telomerase inhibitor, imetelstat, being studied by Geron and Janssen in a Phase 2 study to treat intermediate-2 or high-risk in patients with myelofibrosis.
- Momelotinib, a JAK1, JAK2, ACVR1 inhibitor acquired by Sierra Oncology from Gilead Inc., is in development for treatment of myelofibrosis. Momelotinib has been investigated in two completed Phase 3 trials for the treatment of myelofibrosis.
- Constellation Pharmaceuticals's BET inhibitor, CPI-0610, is in Phase 2 clinical development to treat patients with myelofibrosis in a second-line setting.

Therapies for Treating Muscle Loss

We are currently studying ACE-083 in a Phase 2 clinical trial for the treatment of patients with FSHD, as well as a Phase 2 clinical trial with ACE-083 in patients with CMT. A potential competitor of ACE-083 in CMT is PXT3003, which is an investigational pleotherapy being developed by Pharnext. Pharnext has reported that PXT3003 met the primary endpoint in a Phase 3 trial in patients with CMT1A and based on these data Pharnext intends to file for market approval in the U.S. and Europe.

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We are also aware of approaches to treat other muscle loss diseases that are in clinical trials. Regeneron is developing two drugs in combination, REGN2477 (garetosmab, an activin A antibody, combined with trevogrumab, a myostatin antibody), in a Phase 1 clinical trial to treat muscle wasting diseases. Roche is studying RO7239361, a myostatin fusion protein, in a Phase 1/2 clinical trial of Duchenne muscular dystrophy (DMD). Other approaches to myostatin inhibition, including monoclonal antibodies (such as SRK-015 in Phase 1/2 clinical trials by Scholar Rock), and ligand traps (such as RG6206 in Phase 2/3 clinical trial by Roche and ALG-801 in Phase 1 by Alivegen in partnership with Biogen), are being studied to treat a number of neuromuscular diseases, including muscular dystrophies, disuse muscle atrophy, cancer-related cachexia, and sarcopenia. Nationwide Children's Hospital, in collaboration with The Myositis Association, Parent Project Muscular Dystrophy and Milo Biotechnology, have completed 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) and have a second clinical trial in Duchenne muscular dystrophy underway. There are also other programs in early stage development that focus on gene editing and next generation antisense that could compete with our therapies for treating muscle loss.

Pulmonary Arterial Hypertension

We are currently enrolling the PULSAR Phase 2 clinical trial of sotatercept for the treatment of patients with PAH with preliminary results expected in the first half of 2020, and we recently initiated an exploratory study, called SPECTRA, in the first quarter of 2019 to provide us with further understanding of sotatercept's impact on PAH. PAH is a rare and chronic, rapidly progressing disorder characterized by the constriction of small pulmonary arteries, resulting in abnormally high blood pressure in the pulmonary arteries.

If sotatercept is approved for the treatment of patients with PAH, it would compete with four distinct classes of vasodilator therapies:

- Phosphodiesterase type 5 (PDE5) inhibitors Adcira® (tadalafil, Eli Lilly) and Revatio® (sildenafil, Pfizer), which are orally available small molecules. PDE5 inhibitors prevent degradation of intracellular cGMP released in response to nitric oxide (NO), resulting in relaxation of pulmonary vessels.

- Soluble guanylate cylase (sGC) stimulator Adempas® (riociguat, Bayer), which targets different molecules in the same biological pathway as PDE5 inhibitors and is also an oral small molecule.

- Endothelin receptor antagonists (ERA) Letairis® (ambrisentan, Gilead), Opsumit® (macitentan, Actelion/J&J), and Tracleer® (bosentan, Actelion/J&J)), which are all orally available small molecules. ERAs block activity of endothelin-1, which causes constriction of pulmonary vessels.

- Prostacyclin analogues relax pulmonary vessels, prevent platelet aggregation, and inhibit smooth muscle proliferation. They are the most potent therapies for treating PAH and are available orally (Orenitram® (trepostinil, United Therapeutics), Uptravi® (selexipag, Actelion/J&J)); for inhalation (Tyvaso® (trepostinil, United Therapeutics), Ventavis® (iloprost, Actelion/J&J)); and for infusion (Remodulin® (trepostinil, United Therapeutics), Veletri® (epoprostenol, Actelion/J&J)).

In addition, agents with novel mechanisms of action are being investigated for treatment of patients with PAH:

- Reata Pharmaceuticals and Complexa Inc. are developing Nrf2 modulators bardoxolone and CXA-10, respectively. Reata is evaluating bardoxolone in a phase 3 trial in patients with PAH associated with connective tissue disease. Complexa is evaluating CXA-10 in a phase 2 trial in patients with PAH.
- PhaseBio is evaluating a VPAC peptide PB1046 in a phase 2 trial in patients with PAH.
- Two companies are evaluating agents that are intended to enhance BMPR2 signaling in patients with PAH. Vivus Inc. is evaluating tacrolimus in a phase 2 trial in patients with PAH. Morphogen IX Ltd. is in the process of preclinical development of a protein-engineered variant of BMP9, MGX292, for eventual clinical evaluation in patients with PAH.

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 in North America with our collaboration partner, Celgene, for both luspatercept and, outside of the PH field, sotatercept, and under the terms of our agreements with Celgene, our commercialization costs will be entirely funded by Celgene as approved in the budget agreed to between us and Celgene. We also currently retain worldwide

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commercialization rights for ACE-083, sotatercept in the PH field, and ACE-2494. We intend to build hematology, neuromuscular and pulmonary 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 therapeutic candidates, 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 Regulation".

Our patenting strategy is focused on our therapeutic candidates. 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 708 issued patents and approximately 505 pending patent applications, with pending and issued claims relating to all of our current clinical stage therapeutic candidates, sotatercept, luspatercept, ACE-083 and ACE-2494. 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 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 and pending applications with respect to our clinical stage therapeutic candidates will expire on dates ranging from 2026 to 2037, 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 therapeutic candidates 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:

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Luspatercept Patent Coverage

We hold two issued patents covering the luspatercept 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 Europe, Australia, Canada, 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 two issued patents covering the treatment of anemia by administration of luspatercept in the United States and similar patents issued or pending in other major jurisdictions worldwide, including Europe, Australia, Canada, 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.

We also hold patent applications directed to a variety of other uses for luspatercept. The expected expiration date for these method of treatment patents ranges from 2029 to 2037 exclusive of possible patent term extensions.

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 Australia, Canada, Japan, China, South Korea, Brazil, Mexico, Russia, Israel and India. The expected expiration date for these composition of matter patents is 2026, exclusive of possible patent term extensions.

We hold one pending patent application covering the treatment of pulmonary arterial hypertension by administration of sotatercept in the United States and similar pending applications in other major jurisdictions worldwide, including Europe, Australia, Canada, Japan, South Korea, Brazil, Mexico and Russia. If issued, the expected expiration date for these method of treatment patents is 2037, exclusive of possible patent term extensions,

We also hold patents and patent applications directed to a variety of other uses for sotatercept, including the treatment of anemia. The expected expiration date for these method of treatment patents ranges from 2026 to 2029 exclusive of possible patent term extensions.

ACE-083 Patent Coverage

We hold two issued patents covering the ACE-083 composition of matter in the United States, which are expected to expire in 2029 and 2035, respectively, exclusive of possible patent term extensions. We hold additional pending patent applications covering the ACE-083 composition of matter in many other major jurisdictions worldwide, including Europe, Australia, Canada, Japan, China, South Korea, Brazil, Mexico, Russia and India. The expected expiration date for these patent applications, should they issue as patents, is 2035, exclusive of possible patent term extensions.

We also hold patent applications directed to a variety of uses for ACE-083, including the treatment of muscular dystrophies, such as facioscapulohumeral muscular dystrophy and Charcot-Marie-Tooth disease. The expected expiration date for these method of treatment patent applications, should they issue as patents, is 2035, exclusive of possible patent term extensions.

ACE-2494 Patent Coverage

We hold one issued patent and one pending patent application covering the ACE-2494 composition of matter in the United States, which, if the pending patent application issues, are expected to expire in 2036 and 2037, respectively, exclusive of possible patent term extensions. We hold additional pending patent applications covering the ACE-2494 composition of matter in many other major jurisdictions worldwide, including Europe, Australia, Canada, Japan, China, South Korea, Brazil, Mexico and India. The expected expiration date for these patent applications, should they issue as patents, ranges from 2036 to 2037, exclusive of possible patent term extensions.

We also hold patent applications directed to a variety of uses for ACE-2494, including the treatment of systemic muscle disorders. The expected expiration date for these method of treatment patent applications, should they issue as patents, ranges from 2036 to 2037, exclusive of possible patent term extensions.

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

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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

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, luspatercept and the discontinued program ACE-031, which we refer to as the ActRIIB Agreement. 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 luspatercept. 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 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.

In October 2012, Salk filed a lawsuit against us alleging that we breached the ActRIIB Agreement. In July 2014, we settled the Salk lawsuit and entered into an amendment to the ActRIIB Agreement with Salk. Pursuant to the settlement, we made a one-time total payment of $5 million, inclusive of interest, to Salk and we agreed to pay Salk 6% of future development milestone payments received under the agreement with Celgene relating to luspatercept. Finally, we and Salk have further agreed that the royalty percentage on net sales of luspatercept will remain at 1% as provided in the ActRIIB Agreement with Salk, and that such royalty will be payable until June 2022.

Government Regulation

The preclinical studies and clinical testing, manufacture, labeling, storage, record keeping, advertising, promotion, export, marketing and sales, among other things, of our 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, luspatercept, ACE-083 and ACE-2494 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. Therapeutic candidates 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 therapeutic candidates 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 the safety and efficacy of the biological product for its intended use;
- submission to the FDA of a BLA;

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- 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 therapeutic candidate.

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.

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 trials usually involve 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 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 (PDUFA), as re-authorized most recently in August 2017 (PDUFA VI), the fees payable to the FDA for reviewing a BLA, as well as annual program fees for approved products, can be substantial. For fiscal years 2018-2022, user fees for review of an application that requires clinical data, such as a BLA, plus prescription drug program fees, are estimated at

approximately $2.7 million, subject to certain limited deferrals, waivers, and reductions that may be available, including waiver of the application fee for a product designated for an orphan indication. 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

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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 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 therapeutic candidates under development.

As part of the 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. Since the enactment of the BPCI, the FDA 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 and has approved fewer than ten such products to date. 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 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. Luspatercept has orphan drug designation in the United States for the treatment of beta-thalassemia and for the treatment of MDS.

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

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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. In May 2014, the FDA published a 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 as an amendment to an IND. FDA has already granted this designation to nearly 200 new drugs and has approved more than 50 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 payers, such as government health programs, commercial insurance and managed healthcare organizations. These third-party payers are increasingly challenging the prices

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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 healthcare products. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the cost-effectiveness of our products. If third-party payers do not consider our products to be cost-effective compared to other therapies, the payers 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 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 manufacturer-reported average manufacturer price increases more than inflation and if a manufacturer enters into a supplemental rebate agreement with a specific state Medicaid program.

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 and infused drugs administered by a licensed medical provider in hospital outpatient departments and in the physician office setting. 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). FSS 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 United States and state governments continue to propose and pass legislation designed to reform delivery of, or payment for, health care, which include initiatives to reduce the cost of healthcare. For example, in March 2010, the United States Congress enacted the Patient Protection and Affordable Care Act and the Health Care and Education Reconciliation Act (“Healthcare Reform Act”) which includes changes to the coverage and reimbursement of drug products under government health care programs. Under the Trump administration, there have been ongoing efforts to modify or repeal all or certain provisions of the Healthcare Reform Act. The Trump administration may also take

executive action in the absence of legislative action. For example, in October 2017, the President announced that his administration will withhold the cost-sharing subsidies paid to health insurance exchange plans serving low-income enrollees. Actions by the administration are widely expected to lead to fewer Americans having more comprehensive health insurance compliant with the Healthcare Reform Act, even in the absence of a legislative repeal. Tax reform legislation was also enacted at the end of 2017 that includes provisions that will affect healthcare insurance coverage and payment, such as the elimination of the tax penalty for individuals who do not maintain sufficient health insurance coverage beginning in 2019 (the so-called “individual mandate”). In a November, 2017 report, the Congressional Budget Office estimates that the elimination will increase the number of uninsured by 4 million in 2019 and 13 million in 2027.

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Recently, there has been considerable public and government scrutiny in the U.S. of pharmaceutical pricing and proposals to address the perceived high cost of pharmaceuticals. There have also been several recent state legislative efforts to address drug costs, which generally have focused on increasing transparency around drug costs or limiting drug prices or price increases. Adoption of new legislation at the federal or state level could affect demand for, or pricing of, our product candidates if approved for sale.

We cannot predict the ultimate content, timing or effect of any changes to the Healthcare Reform Act or other federal and state reform efforts. There is no assurance that federal or state health care reform will not adversely affect our future business and financial results.

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 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 payers are challenging the prices charged for medical products and services, and many third-party payers limit reimbursement for newly-approved healthcare 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 therapeutic candidates. Whether or not we obtain FDA approval for a 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 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.

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Fraud and Abuse Laws

Although we currently have no products approved for commercial sale, we may be subject to various federal and state laws pertaining to health care "fraud and abuse," including anti-kickback laws and false claims laws if any of our product candidates may in the future receive regulatory and marketing approval. Anti-kickback laws generally prohibit a prescription drug manufacturer from soliciting, offering, receiving, or paying any remuneration to generate business, including the purchase or prescription of a particular drug. Although the specific provisions of these laws vary, their scope is generally broad and there may not be regulations, guidance or court decisions that apply the laws to particular industry practices. There is therefore a possibility that our practices might be challenged under such anti-kickback laws. False claims laws prohibit anyone from knowingly and willingly presenting, or causing to be presented, any claims for payment for reimbursed drugs or services to third party payers (including Medicare and Medicaid) that are false or fraudulent. Violations of fraud and abuse laws may be punishable by criminal or civil sanctions, including fines and civil monetary penalties, and/or exclusion from federal health care programs (including Medicare and Medicaid).

Laws and regulations have been enacted by the federal government and various states to regulate the sales and marketing practices of pharmaceutical manufacturers with marketed products. The laws and regulations generally limit financial interactions between manufacturers and health care providers and/or require disclosure to the government and public of such interactions. Many of these laws and regulations contain ambiguous requirements or require administrative guidance for implementation. Given the lack of clarity in laws and their implementation, any future activities (if we obtain approval and/or reimbursement from federal healthcare programs for our product candidates) could be subject to the penalty provisions of the pertinent laws and regulations.

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 luspatercept, ACE-083 and ACE-2494. 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 therapeutic candidates.

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 37 full time employees focus on our process development and manufacturing activities. We believe that our strategic investment in manufacturing capabilities allows us to advance our 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. This structure enables us to efficiently transfer preclinical 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 therapeutic candidates. We outsource fill-finish, packaging, labeling, shipping, and distribution.

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We manufacture our therapeutic candidates using readily available raw materials and well established manufacturing procedures based on a standardized process modified for each of our therapeutic candidates. We produce our proteins in bioreactors using Chinese hamster ovary cells that have been genetically engineered to produce our specific therapeutic candidates. We then purify the proteins using industry standard methods, which include affinity chromatography and ultrafiltration operations.

We believe that we can scale our manufacturing processes to support our clinical development programs and the potential commercialization of our therapeutic candidates. For our early phase 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. For the luspatercept Phase 3 clinical trials, we have transferred the process for Phase 3 production to Celgene, under the terms of our collaboration agreements. Celgene uses contract manufacturers for Phase 3 supply of luspatercept, and we expect Celgene will use a contract manufacturer for commercial supply of luspatercept. We also previously successfully transferred the manufacturing process for sotatercept to Celgene, and we expect Celgene will use a contract manufacturer for additional clinical supply and any future commercial supply of sotatercept. We intend to contract with a third party manufacturer for the supply of ACE-083 and ACE-2494 for any Phase 3 clinical trials.

Employees

As of December 31, 2018, we had 173 full-time employees, 122 of whom are involved in research, development or manufacturing, and 43 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.

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 address is www.acceleronpharma.com. The contents of our website are not part of this Annual Report on Form 10-K. We make available free of charge through our website our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to these reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, as soon as reasonably practicable after we electronically file or furnish such materials to the Securities and Exchange Commission.

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Item 1A. Risk Factors

Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below in addition to the other information included or incorporated by reference in this Annual Report on Form 10-K before purchasing our common stock. If any of the following risks actually occurs, our business, financial condition or results of operations would likely suffer, possibly materially. In that case, the trading price of our common stock could fall, and you may lose all or part of the money you paid to buy our common stock. 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 may 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 December 31, 2018, we had an accumulated deficit of $586.5 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. 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 ACE-083, ACE-2494 or other therapeutic candidates. If we do not receive the anticipated milestone payments or do not enter into partnerships for ACE-083, ACE-2494 or other 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 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 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 may 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 December 31, 2018, our cash, cash equivalents and investments were $291.3 million. In January 2019, we raised an additional $248.2 million in net proceeds in connection with our offering of 6,151,163 shares of our common stock. We believe that we will continue to expend substantial resources for the foreseeable future developing sotatercept in pulmonary hypertension, which we refer to as the PH field, ACE-083, ACE-2494 and new 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 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 therapeutic candidates.

Celgene generally pays development, manufacturing and commercialization and certain patent costs for luspatercept and for sotatercept outside of the PH field as approved in the budgets agreed to between us and Celgene for each program. From time to time, we may also elect to conduct additional activities to support luspatercept at our own expense. Other than those costs, our future capital requirements depend on many factors, particularly in connection with the development of our other therapeutic candidates including sotatercept in the PH field, ACE-083 and

ACE-2494:

- the scope, progress, results and costs of researching and developing our other therapeutic candidates, and conducting preclinical studies and clinical trials;

- the timing of, and the costs involved in, obtaining regulatory approvals for our other therapeutic candidates if clinical trials are successful;

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- the cost of commercialization activities for our other therapeutic candidates, if any of these therapeutic candidates is approved for sale, including marketing, sales and distribution costs;

- the cost of manufacturing our other 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.

Our current 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 that 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 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 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 therapeutic candidates on terms unfavorable 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 therapeutic candidates, 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 sotatercept in the PH field, ACE-083, ACE-2494 or any therapeutic candidates other than luspatercept or sotatercept outside of the PH field, or grant rights to develop and market therapeutic candidates that we would otherwise prefer to develop and market ourselves.

Risks Related to Regulatory Review and Approval of Our Therapeutic Candidates

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

Our 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 therapeutic candidates, we or our partners must demonstrate through extensive preclinical studies and clinical trials that the 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 luspatercept, sotatercept, ACE-083, ACE-2494 or any other therapeutic candidate in some but not all of the territories available or some but not all of the target indications or may receive approval with limited labeling or boxed warnings, resulting in limited commercial opportunity for the approved therapeutic candidates, or we or they may never obtain regulatory approval for these therapeutic candidates.

Delays in the commencement, enrollment or completion of clinical trials of our 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 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:

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- delays by us or our current or future 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 or manufacturing concerns or after an inspection of clinical operations or trial sites;
- failure by CROs, other third parties or us or our current or future 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 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 therapeutic candidates that are viewed to outweigh its potential benefits;
- delays resulting from the FDA's inability to timely review and process any submissions we or Celgene have filed during the pendency of a whole or partial U.S. government shutdown; or
- 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 of our therapeutic candidates, we will not be able to obtain regulatory approval and will not be able to commercialize our therapeutic candidates.

There is a high risk of clinical failure at any stage of clinical development, and we may never succeed in developing marketable products or generating product revenue.

Our encouraging preclinical and clinical results to date for luspatercept, sotatercept, and ACE-083, and our encouraging preclinical results to date for ACE-2494, 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 current or future partners' ongoing or future clinical trials are inconclusive with respect to the efficacy of our 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 therapeutic candidates, we or our partner may be prevented or delayed in obtaining marketing approval for our therapeutic candidates. We routinely develop our therapeutic candidates in multiple indications and our therapeutic candidates are at multiple stages of development at any given time, and any data, including safety or efficacy data, from any of our clinical trials could have a negative effect on our other clinical trials for the same or different therapeutic candidates. For example, if we or Celgene observe negative data in any one or more of our luspatercept clinical trials, this data could have an adverse effect on our ability to

complete the MEDALIST or BELIEVE Phase 3 clinical trials or obtain regulatory approval for luspatercept in any indication.

In addition, data obtained from trials and studies, including extension 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, regulators may ask us to conduct more rigorous studies or trials or studies with endpoints that are different from the studies we are currently conducting. Successful achievement of study endpoints does not guarantee progression to further clinical development, receipt of regulatory approval or commercialization. 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

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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 risk evaluation and mitigation strategy.

If we or our current or future 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 current or future partners intend to market our 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 therapeutic candidate 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 current or future 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.

We and, for our Celgene partnered programs, Celgene, regularly request and receive guidance from the FDA and foreign regulators regarding the design or conduct of clinical trials with our therapeutic candidates. This guidance is not binding on these agencies and their policies and guidance could change substantially and unpredictably, potentially in a way that makes our clinical trials or our path to regulatory approval longer, more expensive or otherwise more difficult.

Any guidance that we or Celgene receive from the FDA or foreign regulators regarding the design or conduct of our or Celgene's clinical trials is not necessarily indicative of what these regulators will eventually require from us or Celgene to obtain regulatory approval of our therapeutic candidates. These regulators typically caution that any guidance received from them represents their then-current thinking, does not create or confer any rights to us or Celgene, and does not operate to bind the regulator. If later guidance that we or Celgene receive from the FDA or foreign regulators regarding our clinical trial design or conduct is materially different than the current guidance we have received from these regulators, we may need to change our clinical development plans and it may take longer, be more expensive or otherwise be more difficult to obtain FDA or foreign regulatory approval of our therapeutic candidates and our business may be materially harmed.

We undertake no obligation to disclose guidance that we or Celgene may receive from the FDA or foreign regulators. Any guidance from the FDA or foreign regulators that we may disclose publicly speaks only as of the date of such disclosure. We undertake no obligation to update any disclosure we make regarding regulator guidance to reflect additional regulatory guidance received after the date of such disclosure or to reflect the occurrence of unanticipated events that may affect the guidance.

Even if we or our current or future partners receive regulatory approval for our therapeutic candidates, such products will be subject to ongoing regulatory review, which may result in significant additional expense. Additionally, our therapeutic candidates, if approved, could be subject to labeling and other restrictions, and we or our current or future 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 current or future partners receive for our 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 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 therapeutic candidate, 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;

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- 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 policies of the FDA and other regulatory agencies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our 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 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.

A Fast Track designation by the FDA may not actually lead to a faster development or regulatory review or approval process.

In the United States, luspatercept received Fast Track designation for the treatment of anemia in patients with lower-risk myelodysplastic syndromes, or MDS, for the treatment of patients with transfusion-dependent beta-thalassemia, and for the treatment of patients with non-transfusion-dependent beta-thalassemia. The FDA grants Fast Track designation to therapies that are considered capable of addressing unmet medical needs and possess the potential to treat serious or life-threatening disease conditions in order to facilitate its development and expedite the review procedure. The FDA has broad discretion in granting Fast Track designation, so even if we believe that a particular product candidate is eligible for such designation, the FDA could decide not to grant it. Even though luspatercept has received Fast Track designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may also withdraw Fast Track designation if it believes that the designation is no longer supported by data from our clinical development program.

The ongoing clinical trials with luspatercept may be delayed, suspended or terminated, or may not lead to marketing approval.

Subsequent to the positive readout of primary and secondary endpoints in 2018 in the Phase 3 MEDALIST and BELIEVE trials, Celgene is currently continuing these trials per protocol for the purpose of obtaining longer-term data regarding the safety and efficacy of luspatercept in these patient populations. In addition to the MEDALIST and BELIEVE Phase 3 clinical trials with luspatercept, Celgene is currently conducting a Phase 2 clinical trial in non-transfusion-dependent beta-thalassemia patients, referred to as the BEYOND trial, with preliminary topline results currently expected in 2020. Celgene has also initiated a Phase 3 clinical trial, the COMMANDS trial, in first-line, lower-risk MDS patients and enrollment is ongoing. Enrollment is also currently ongoing in a Phase 2 clinical trial for the treatment of patients with myelofibrosis, a rare bone marrow disorder, with preliminary topline results currently expected in the second half of 2019. We are also currently conducting two long-term Phase 2 extension studies with luspatercept - one in patients with MDS and another in patients with beta-thalassemia. Celgene or we may experience delays in the conduct of these clinical trials, including delays related to patients withdrawing from the trial, or drug supply. If patients experience adverse events while in clinical trials with luspatercept, then one or more of these trials may be delayed, suspended or terminated. Celgene may not achieve the remaining longer-term secondary endpoints for one or both of the MEDALIST and BELIEVE trials and may not achieve any of the endpoints in the other ongoing trials. Additionally, we and Celgene have announced that we are planning to evaluate luspatercept in one or more indications beyond MDS, beta-thalassemia and myelofibrosis. Even though the primary endpoint and key secondary endpoints were achieved in the MEDALIST and BELIEVE trials, one or more health authorities may not approve luspatercept for the desired indications. The MEDALIST and BELIEVE trials were designed with input from health authorities in many different countries, but this guidance is not binding on these regulators, and it may be necessary to conduct one or more additional clinical trials in order to achieve marketing authorization in one or more regulatory jurisdictions. Guidance that we or Celgene receive from the FDA or foreign

regulators regarding the design or conduct of the MEDALIST or BELIEVE clinical trials is not necessarily indicative of what these regulators will eventually require from us or Celgene to obtain regulatory approval of luspatercept in these indications. Any regulatory approvals that we or Celgene receive for luspatercept 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.

If we or any of our current or future partners violate the guidelines pertaining to promotion and advertising of any of our therapeutic candidates, 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

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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: 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 of our current or future partners may inadvertently violate OPDP's guidelines in the future and be subject to an OPDP untitled letter or warning letter, which may have a negative impact on our business.

Risks Related to Our Reliance on Third Parties

We are dependent on Celgene for the successful development and commercialization of sotatercept outside of the PH field and our most advanced therapeutic candidate, luspatercept. If Celgene does not devote sufficient resources to the development of luspatercept, discontinues development of luspatercept, is unsuccessful in its efforts, or chooses to terminate the luspatercept agreement with us, our business will be materially harmed.

We have entered into collaboration agreements with Celgene to develop and commercialize sotatercept and luspatercept. Pursuant to the sotatercept agreement, responsibility for all clinical and other product development activities for sotatercept for all indications outside of the PH field and for manufacturing sotatercept for such indications has been transferred to Celgene. For luspatercept, we are responsible for conducting ongoing Phase 2 clinical trials in MDS and beta-thalassemia, and we are also responsible for manufacturing supplies for our Phase 1 and Phase 2 studies. Celgene will be responsible for all clinical development and manufacturing activities after such studies are completed. Celgene is generally responsible for paying 100% of worldwide development costs for luspatercept and for sotatercept outside of the PH field as approved in the budget agreed to between us and Celgene for each program. We will co-promote luspatercept and, outside of the PH field, sotatercept, if approved by the FDA and its counterparties, in North America, for which our commercialization costs will be entirely funded by Celgene, and from time to time we may elect to conduct additional activities to support commercialization of luspatercept or sotatercept outside of the PH field at our own expense.

Celgene is obligated to use commercially reasonable efforts to develop and commercialize luspatercept and sotatercept outside of the PH field. 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 luspatercept and sotatercept. This may occur for many reasons, including internal business reasons or because of unfavorable regulatory feedback. Further, on review of the safety and efficacy data available to date, the FDA may impose requirements on a clinical trial program that would render the program commercially nonviable. In the event of any such decision, we would be unable to advance such program ourselves.

Under our collaboration agreements, when Celgene takes over development activities of a therapeutic candidate, it may determine the development plan and activities for that 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 luspatercept and, outside of the PH field, sotatercept, 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, other than sotatercept in the PH field. More broadly, if Celgene elects to discontinue the development of sotatercept outside of the PH field and/or luspatercept, we may be unable to advance the products ourselves.

Pursuant to our collaboration agreement with Celgene for the development of sotatercept in the PH field, we will rely on Celgene for many aspects of our development of sotatercept in the PH field, including, for example, regulatory support. If Celgene fails to perform its obligations under the sotatercept agreement, our ability to develop sotatercept

in the PH field may be materially harmed.

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

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- 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 therapeutic candidates by Celgene.

- Celgene may develop and commercialize, either alone or with others, products that are similar to or competitive with the therapeutic candidates that are the subject of its partnerships with us.

- 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.

- Celgene may develop or commercialize our 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 may 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 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 luspatercept 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 if we choose not to, or are unable to, enter into a new collaboration for these candidates.

- 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. For example, on January 2, 2019, Celgene entered into a merger agreement with Bristol-Myers Squibb Company, or BMS, and a wholly-owned subsidiary of BMS, or the Merger Sub, pursuant to which Celgene is to merge into the Merger Sub and become a wholly-owned subsidiary of BMS, subject to the satisfaction of customary closing conditions, including approval of the proposed merger by the stockholders of Celgene and BMS.

- We and Celgene routinely publicly disclose information about luspatercept and sotatercept, and if our and Celgene’s public disclosures are inconsistent, this could materially harm public and market perception of luspatercept and sotatercept and the value of our common stock.

Through a variety of public forums and media, such as press releases, conference calls, filings with the Securities and Exchange Commission, or SEC, and scientific/medical conferences, we and Celgene routinely disclose information about luspatercept and sotatercept. We and Celgene may not agree on information that is disclosed or the interpretation of that information, and our disclosures may be inconsistent with Celgene's disclosures. If our and Celgene's public disclosures are inconsistent, public and market perception of luspatercept and sotatercept and the value of our common stock could be materially adversely affected.

- We currently have limited marketing, sales and distribution experience and capabilities and, for luspatercept and, outside of the PH field, sotatercept, we will be dependent upon Celgene for commercialization.

For luspatercept and, outside of the PH field, sotatercept, we and Celgene share commercialization obligations in the United States and we are solely dependent on Celgene for commercialization outside of the United States. As a

company without any commercial products, we have very limited marketing, sales and distribution experience and capabilities in the United States. To successfully commercialize luspatercept and, outside of the PH field, sotatercept, in the United States, we will need to rely extensively on Celgene, and we will need to establish our own adequate marketing, sales and distribution capabilities. In addition, to successfully commercialize our wholly-owned therapeutic candidates and sotatercept in the PH field in jurisdictions where they may be approved, we will need to establish our own marketing, sales and distribution capabilities. Failure to establish these capabilities, whether due to insufficient resources or some other cause, will limit or potentially halt our ability to successfully commercialize any therapeutic candidates, and will adversely affect our financial results. Even if we

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do develop such capabilities, we will compete with other companies that have more experienced and well-funded marketing, sales and distribution operations.

We and Celgene rely on third parties to conduct preclinical studies and clinical trials for our 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 therapeutic candidates.

We design the clinical trials for sotatercept outside of the PH field, ACE-083 and ACE-2494, and will do so for any future unpartnered therapeutic candidates, and we will continue to work with Celgene on any ongoing or future trials for luspatercept and sotatercept in the PH field. 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 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 therapeutic candidates may not meet regulatory requirements or may be delayed. 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 therapeutic candidates on a timely basis or at all.

In addition to our internal manufacturing, we rely on third-party manufacturers in the production and testing of our therapeutic candidates, and any failure by a third-party manufacturer may delay or impair our ability to complete clinical trials or commercialize our 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. For Phase 2 and Phase 3 clinical trials of sotatercept in the PH field and for Phase 3 clinical trials 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 therapeutic candidates is highly cyclical, with periods of relatively abundant capacity alternating with periods in which there is little available capacity. If any need we have for contract manufacturing services increases during a period of industry-wide tight capacity, we 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 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 agree. In addition, any delay in contracting for fill & finish services, or failure of the contract manufacturer to perform the services as needed, may impair or render unusable the patient data from then-ongoing clinical trials and/or delay clinical trials, registration and launches. Any such issues may have a substantial negative effect on our business.

For sotatercept and our most advanced therapeutic candidate, luspatercept, we rely on our collaboration partner Celgene to manufacture, or contract for the manufacture of, bulk drug substance and finished drug product for use in

late stage clinical trials and for commercial supplies of these product candidates, if approved. 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 luspatercept, if approved.

Celgene is responsible for manufacturing luspatercept and sotatercept for all Celgene-sponsored clinical trials. Celgene generally does not perform the manufacture of the drug substance or drug product for either luspatercept or sotatercept itself. Celgene has used and may continue to use contract manufacturers for the manufacture of drug substance and drug product for

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luspatercept and sotatercept, and we have no expectation that Celgene plans to perform the manufacture of bulk drug substance or drug product for either luspatercept or sotatercept in the future. However, Celgene would have the right to manufacture luspatercept or sotatercept outside of the PH field for clinical and commercial supply and in the PH field for commercial supply, itself or through the use of contract manufacturers. We understand that Celgene has entered into manufacturing arrangements for clinical and commercial supplies of sotatercept and luspatercept bulk drug substance with contract manufacturers with considerable biotherapeutics manufacturing experience, including manufacturing monoclonal antibodies through processes similar to those used for sotatercept. If any of these manufacturers is unwilling or unable to manufacture sufficient quantities of sotatercept and/or luspatercept to meet clinical or commercial demand, either for technical or business reasons, the development and commercialization of sotatercept and/or luspatercept may be delayed.

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, part of our strategy is to evaluate and enter into additional partnerships in the future for our other product candidates when strategically attractive, including potentially with major biotechnology or pharmaceutical companies. We face significant competition in seeking appropriate partners for our therapeutic candidates, and the negotiation process is time-consuming and complex. In order for us to successfully partner our therapeutic candidates, potential partners must view these 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 therapeutic candidate is delayed or sales of an approved product are disappointing. Any delay in entering into new strategic partnership agreements related to our other therapeutic candidates could delay the development and commercialization of these therapeutic candidates and reduce their competitiveness even if they reach the market.

If we fail to establish and maintain additional strategic partnerships related to ACE-083, ACE-2494 or other therapeutic candidates, we will bear all of the risk and costs related to the development of any such 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 therapeutic candidate.

Risks Related to Our Intellectual Property

If we are unable to obtain or protect intellectual property rights related to our 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 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 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 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 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 therapeutic candidates fail to issue, if their breadth or strength of protection is threatened, or if they fail to provide meaningful exclusivity for our therapeutic candidates, it could dissuade companies from collaborating with us. We regularly file patent applications to cover our therapeutic candidates. 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 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 therapeutic candidate that we or our current or future 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 therapeutic candidate.

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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 therapeutic candidate under patent protection could be reduced. Even if patents covering our 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 current or future partners may be unable to prevent competitors from entering the market with a product that is similar to or the same as our therapeutic candidates. In addition, the royalty we would receive under our collaboration agreements with Celgene for sotatercept and luspatercept 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 current or future 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 current or future partners are developing and may develop our therapeutic candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our 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 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 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 therapeutic candidates or the use or manufacture of our 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 therapeutic candidate until such patent expired or unless we or our partners obtain a license. These 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 luspatercept, 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 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 therapeutic candidates, and we may be required to pay damages.

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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 therapeutic candidates, programs, or intellectual property could be diminished. Accordingly, the market price of our common stock could decline.

We have in-licensed, and may in the future in-license, 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. As part of our discovery and development activities, we routinely evaluate in-licenses from academic and research institutions. See "Business–Intellectual Property–In-Licenses" for a description of our license agreements.

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 therapeutic candidate, may be adversely affected.

If we do not obtain patent term extension and data exclusivity for any product candidates we may develop, our business may be materially harmed.

Depending upon the timing, duration and specifics of any FDA marketing approval of any product candidates we may develop, one or more of our owned or licensed U.S. patents may be eligible for limited patent term extension under the Hatch-Waxman Act. Similar extensions as compensation for patent term lost during regulatory review processes are also available in certain foreign countries and territories, such as in Europe under a Supplementary Patent Certificate. However, we may not be granted an extension in the United States and/or foreign countries and territories because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is shorter than what we request or we fail to choose the most optimal patents to extend, our competitors may obtain approval of competing products following our patent expiration, and our business, financial condition, results of operations and prospects could be materially harmed.

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 Development and Commercialization of Our Therapeutic Candidates

Our future commercial success depends upon attaining significant market acceptance of our therapeutic candidates, if approved, among physicians, patients, healthcare payers and acceptance by the operators of major medical providers.

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Even if we or our current or future partners obtain regulatory approval for any of our existing therapeutic candidates or any therapeutic candidates that we may develop or acquire in the future, the product may not gain market acceptance among physicians, healthcare payers, 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;
- decisions by healthcare organizations to utilize the product;
- 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;
- relative convenience and ease of administration;
- the prevalence and severity of adverse side effects; and
- the effectiveness of our and our current or future partners' sales and marketing efforts.

Market acceptance is critical to our ability to generate significant revenue. Any 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 therapeutic candidates, which could make it difficult for us to sell our products profitably.

Market acceptance and sales of any approved therapeutic candidates will depend significantly on the availability of adequate coverage and reimbursement from third-party payers and may be affected by existing and future healthcare reform measures. Government authorities and third-party payers, 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 payer'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 current or future 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 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 healthcare 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.

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Price controls and price pressure may be imposed in foreign and U.S. 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, including those in the United States, 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 current or future partners may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our therapeutic candidates 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.

Recent and future healthcare reform legislation and other changes in the healthcare industry and in healthcare spending 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 healthcare availability, the method of delivery or payment for healthcare products and services could negatively impact our business, operations and financial condition. There is significant interest in promoting healthcare 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, and as evidenced by public discourse on the topic. See "Business–Government Regulation" for a detailed description on recent developments in healthcare regulations. It is likely that federal and state legislatures within the United States and foreign governments will continue to consider changes to existing healthcare 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:

- public and market perceptions of our future business prospects, including future revenue and profitability;
- 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 therapeutic candidates. Our objective is to design, develop and commercialize new products with superior efficacy, convenience, tolerability and safety. In many cases, the therapeutic candidates that we commercialize with our strategic partners or on our own will compete with existing, market-leading products. See "Business–Competition" for a detailed description of the competitive landscape for our therapeutic candidates.

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 therapeutic candidates 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 therapeutic candidates before we do. In addition, any new product that competes

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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.

If our clinical trials fail to demonstrate the safety and efficacy of our therapeutic candidates to the satisfaction of regulatory authorities or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our therapeutic candidates.

Undesirable side effects caused by our therapeutic candidates 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 clinical trials for our clinical stage therapeutic candidates. Serious adverse events deemed to be caused by our therapeutic candidates could have a material adverse effect on the development of our therapeutic candidates and our business as a whole. In the case of placebo-controlled clinical trials, if the rate of an adverse event or serious adverse event observed in the treatment group exceeds the rate of such adverse event or serious adverse event observed in the placebo-controlled group, then the FDA or other regulatory authorities may require the delay or termination of such clinical trial, or require the conduct of one or more additional clinical trials to further demonstrate the safety of the therapeutic candidate.

For a more complete description of the safety profile for our therapeutic candidates, see the description of each of our therapeutic candidates in the "Business" section of this Annual Report on Form 10-K.

Our understanding of the relationship between our 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 therapeutic candidates will not be observed. As is typical in drug development, we have a program of ongoing toxicology studies in animals for our clinical stage therapeutic candidates 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.

Before obtaining marketing approval from regulatory authorities for the sale of our therapeutic candidates, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our therapeutic candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. In addition, preclinical and clinical data are often susceptible to varying interpretations and analyses, and successful achievement of study endpoints does not guarantee progression to further clinical development, receipt of regulatory approval or commercialization. Many companies that have believed their therapeutic candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products.

We or our current or future partners may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our therapeutic candidates, including:

- regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may have delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- clinical trials of our therapeutic candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
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the number of patients required for clinical trials of our therapeutic candidates may be larger than we anticipate; enrollment in these clinical trials may be slower than we anticipate; or participants may drop out of these clinical trials at a higher rate than we anticipate;

- third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;

- we might have to suspend or terminate clinical trials of our therapeutic candidates for various reasons, including a finding that the participants are being exposed to unacceptable health risks;

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- regulators, institutional review boards, or the data safety monitoring board for such trials may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;

- the cost of clinical trials of our therapeutic candidates may be greater than we anticipate;

- the supply or quality of our therapeutic candidates or other materials necessary to conduct clinical trials of our therapeutic candidates may be insufficient or inadequate; and

- our therapeutic candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or institutional review boards to suspend or terminate the trials.

If we or our current or future partners are required to conduct additional clinical trials or other testing of our therapeutic candidates beyond those that we currently contemplate, if we or our current or future partners are unable to successfully complete clinical trials of our therapeutic candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if we or others identify undesirable side effects caused by our therapeutic candidates either before or after receipt of marketing approval, then a number of potentially significant negative consequences could result, including that we or our current or future partners may:

- be delayed in obtaining or be unable to obtain marketing approval for our therapeutic candidates;

- obtain approval for indications or patient populations that are not as broad as intended or desired;

- be required to provide a medication guide outlining the risks of such side effects for distribution to patients;

- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings, including boxed warnings;

- suffer reputational harm;

- be sued and held liable for harm caused to patients;

- be subject to additional post-marketing testing requirements; or

- have the product removed from the market after obtaining marketing approval.

Product development costs will also increase if we or our current or future partners experience delays in testing or marketing approvals. We do not know whether any clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our therapeutic candidates, could allow our competitors to bring products to market before we do, and could impair our ability to successfully commercialize our therapeutic candidates, any of which may harm our business and results of operations.

Our results to date do not guarantee that any of our therapeutic candidates will be safe or effective, or receive regulatory approval.

The risk of failure of our current therapeutic candidates is high. To date, the data supporting our clinical development strategy for our therapeutic candidates are primarily derived from laboratory and preclinical studies and limited early-to-mid-stage clinical trials. Later clinical trials may not yield data consistent with earlier clinical trials. Similarly, clinical responses seen in patients enrolled at early stages of a clinical trial may not be replicated in patients enrolled in that trial at a later time. In addition, adverse events not observed in early clinical trials may be seen for the first time in later studies, or adverse events observed in a small number of patients in early trials may be seen in a

greater number of patients in later studies and have greater statistical significance than previously anticipated. In the event that our clinical trials do not yield data consistent with earlier experience, it may be necessary for us to change our development strategy or abandon development of that therapeutic candidate, either of which could result in delays, additional costs and a decrease in our stock price.

Our Phase 2 and Phase 3 clinical trial results for luspatercept are not necessarily indicative or predictive of the future results of Celgene's ongoing Phase 2 or Phase 3 clinical trials. It is impossible to predict when or if any of our therapeutic candidates will prove safe or effective in humans or receive regulatory approval. These therapeutic candidates may not demonstrate in patients the chemical and pharmacological properties ascribed to them in laboratory studies or early-to-mid-

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stage clinical trials, and they may interact with human biological systems or other drugs in unforeseen, ineffective or harmful ways. If we are unable to discover or successfully develop drugs that are safe and effective in humans, we will not have a viable business.

We manufacture ACE-083, ACE-2494, our other unpartnered and preclinical therapeutic candidates, and, for our Acceleron-sponsored trials, luspatercept, at our manufacturing facility. If our manufacturing facility is damaged or destroyed or production at this facility is otherwise interrupted, our business and prospects would be negatively affected.

If the manufacturing facility at our corporate headquarters or the equipment in it is damaged or destroyed, or if production at this facility is otherwise interrupted, we may not be able to quickly or economically replace our manufacturing capacity or replace it at all. In the event of a temporary or protracted loss of this facility or equipment, we might not be able to transfer manufacturing to a third party. Even if we could transfer manufacturing to a third party, the shift would likely be expensive and time-consuming, particularly since the new facility would need to comply with the necessary regulatory requirements and we would need approval from the FDA and foreign regulators before administering any products manufactured at that facility to patients. Such an event could impair or render unusable patient data from then-ongoing clinical trials and/or delay our clinical trials, registration and launches. Any such issues may have a substantial negative effect on our business.

Our expanded research activities may not identify new therapeutic candidates, and we may not be successful in developing any new therapeutic candidates that are identified.

Discovery and development of new therapeutic candidates is an unpredictable activity. We may not succeed in identifying new therapeutic candidates, and if we are unable to do so, our pipeline of clinical stage therapeutic candidates will be reduced in size, potentially harming our business. Our discovery efforts are primarily focused on IntelliTrap™ therapeutic candidates and antibodies. We have limited experience manufacturing and developing antibodies and IntelliTrap™ proteins, and we may not be successful at doing so in the future. Manufacturing biologic therapeutic candidates is complex and often requires extensive process development to achieve suitable quality and quantity of drug substance for clinical development and commercialization, and we may not succeed in achieving the quality and quantity of drug substance that is required at any particular stage. We may be unable to manufacture these therapeutic candidates, these therapeutic candidates may show unacceptable toxicity or pharmacokinetic properties, or these therapeutic candidates may not be safe or effective in clinical trials.

Risks Related to Our Business and Industry

If we undertake business combinations, collaborations or similar strategic transactions, they may disrupt our business, divert management’s attention, dilute stockholder value or be difficult to integrate.

On a regular basis, we consider various business combination transactions, collaborations, license agreements and strategic transactions with third parties, including transactions which may result in us acquiring, or being acquired by, a third party. The consummation or performance of any future business combination, collaboration or strategic transaction may involve risks, such as:

- diversion of managerial attention and resources from day-to-day operations;
- challenges associated with integrating acquired technologies and operations of acquired companies;
- exposure to unforeseen liabilities or increased regulatory and compliance obligations;
- difficulties in the assimilation of different cultures and practices, as well as in the assimilation and retention of broad and geographically dispersed personnel and operations;
- misjudgment with respect to value, return on investment or strategic fit;
- higher than expected transaction costs; and

- additional dilution to our existing stockholders if we issue equity securities as consideration for any acquisitions.

As a result of these risks, we may not be able to achieve the expected benefits of any such transaction. Future business combinations could involve the acquisition of significant intangible assets. We may need to record write-downs from future impairments of identified intangible assets and goodwill. These accounting charges would increase a reported loss or reduce any future reported earnings. In addition, we could use substantial portions of our available cash to pay the purchase price for

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company or product candidate acquisitions. We could also incur debt or issue additional equity securities as consideration for these acquisitions, which could cause our stockholders to suffer significant dilution.

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

We are highly dependent on members of our senior management. The loss or transition of services from any member of our senior management could impede the achievement of our research, development or commercialization objectives.

Recruiting and retaining qualified scientific, clinical, regulatory, 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 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.

We may encounter difficulties in managing our organizational changes and successfully adjusting our operations.

As we seek to advance our 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 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 therapeutic candidates.

We face an inherent risk of product liability as a result of the clinical testing of our 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 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 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. 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

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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 could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against companies following a decline in the market price of their securities. This risk is especially relevant for us because biopharmaceutical companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

Comprehensive tax reform legislation could adversely affect our business and financial condition.

On December 22, 2017, tax legislation commonly known as the "Tax Cuts and Jobs Act" (TCJA) was enacted that significantly reforms the Internal Revenue Code of 1986, as amended. The TCJA, among other things, includes changes to U.S. federal tax rates, imposes significant additional limitations on the deductibility of interest and net operating loss carryforwards, or NOLs, allows for the expensing of capital expenditures, and puts into effect the migration from a "worldwide" system of taxation to a territorial system. Our net deferred tax assets and liabilities have been revalued at the newly enacted U.S. corporate tax rate, and the impact of the reduction to our deferred tax assets and associated valuation allowance was recognized in 2017. We continue to examine the impact this tax reform legislation may have on our business. The impact of this tax reform is uncertain and could be adverse.

Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.

As of December 31, 2018, we had federal NOLs of approximately $556.0 million and state NOLs of approximately $515.0 million available to reduce future taxable income, if any. These federal and state NOL carryforwards generally expire at various times through 2038, however, under the TCJA, federal NOLs generated after December 31, 2017 will not be subject to expiration. Under Section 382 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an "ownership change," generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards, or NOLs, and other pre-change tax attributes (such as research tax credits) to offset its post-change income may be limited. We have completed several financings since our inception which may have resulted in a change in control as defined by IRC Section 382. We may also experience ownership changes in the future as a result of subsequent shifts in our stock ownership. As a result, if we earn net taxable income, our ability to use our pre-change net operating loss carryforwards to offset U.S. federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. Further, the reduction of the corporate tax rate under the TCJA may reduce the potential economic benefit of our NOLS and any other deferred tax assets.

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

We 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 materials that we use in our manufacturing process. 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.

Our relationships with healthcare providers, physicians and third-party payers will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which, in the event of a violation, could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third-party payers will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our future arrangements with

healthcare providers, physicians and third-party payers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any medicines for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following:

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- the federal Anti-Kickback Statute, or AKS, prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation or arranging of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid. Remuneration is not defined in the AKS and has been broadly interpreted to include anything of value, including for example, gifts, discounts, coupons, the furnishing of supplies or equipment, credit arrangements, payments of cash, waivers of payments, ownership interests and providing anything at less than its fair market value;
- the federal False Claims Act and civil monetary penalty laws impose criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, false or fraudulent claims for payment by a federal healthcare program or making a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties, currently set at $11,181 to $22,363 per false claim;
- federal criminal laws that prohibit executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- the federal Food, Drug and Cosmetic Act and its regulations, which prohibit, among other things, the introduction or delivery for introduction into interstate commerce of any drug that is adulterated or misbranded;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the Foreign Corrupt Practices Act, a U.S. law, which regulates certain financial relationships with foreign government officials (which could include, for example, certain medical professionals) and its foreign equivalents;
- the federal Physician Payments Sunshine Act requires applicable manufacturers of covered drugs to report payments and other transfers of value to physicians and teaching hospitals;
- the national anti-bribery laws of European Union Member States, such as the U.K. Bribery Act 2010, or the Bribery Act, which prohibit the provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws and transparency statutes, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payers, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing amount of focus on privacy and data protection issues with the potential to affect our business, including state security breach notification laws, state health information privacy laws and federal and state consumer protection laws, that govern the collection, use and disclosure of personal information. Although we are not directly subject to HIPAA, we could be

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subject to criminal penalties if we knowingly obtain individually identifiable health information from a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA. Other countries also have, or are developing, laws governing the collection, use and transmission of personal information. For example, the collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the EU General Data Protection Regulation (GDPR), which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EU, including the U.S., and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR will be a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with our European activities.

Our internal computer systems, or those of our partners, third-party CROs or other contractors or consultants, may fail or suffer data breaches and cyber-attacks, which could compromise our intellectual property or other sensitive information and could result in a material disruption of our therapeutic candidate development programs.

In the ordinary course of our business, we collect, maintain and transmit sensitive data on our networks and systems and on the networks and systems of our partners, third-party CROs and other contractors or consultants, including our intellectual property and proprietary or confidential business information (such as research data and employee personal information) and confidential information with respect to our vendors and our partners. The secure maintenance of this information is critical to our business and reputation. We believe that companies have been increasingly subject to a wide variety of security incidents, cyber-attacks and other attempts to gain unauthorized access. These threats can come from a variety of sources, ranging in sophistication from an individual hacker to a state-sponsored attack. Cyber threats may be generic, or they may be custom-crafted against our information systems. Over the past few years, cyber-attacks have become more prevalent and much harder to detect and defend against. Our network and storage applications and those of our clinical research organizations, collaborators and vendors may be subject to unauthorized access by hackers or breached due to operator error, malfeasance or other system disruptions. It is often difficult to anticipate or immediately detect such incidents and the damage caused by such incidents. These data breaches and any unauthorized access or disclosure of our information or intellectual property could compromise our intellectual property and expose sensitive business information. A data security breach could also lead to public exposure of personal information of our employees. Cyber-attacks could cause us to incur significant remediation costs, result in product development delays, disrupt key business operations and divert attention of management and key information technology resources. Our network security and data recovery measures and those of our clinical research organizations, collaborators and vendors may not be adequate to protect against such security breaches and disruptions. These incidents could also subject us to liability, expose us to significant expense and cause significant harm to our reputation and business. While we have not experienced any such material security breaches or disruptions to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our or our partners' regulatory approval efforts and significantly increase our costs to recover or reproduce the data.

Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. A severe or prolonged economic downturn could result in a variety of risks to our business,

including, weakened demand for our therapeutic candidates and our ability to raise additional capital when needed on acceptable terms, if at all. Weak global economic conditions, especially in Europe, could decrease the number of clinical trial sites available to us and hinder our ability to conduct clinical trials, which would have a material adverse effect on our business and the development of our therapeutic candidates. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption, or cause our customers to delay making payments for our services. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

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Risks Related to Our Common Stock

The market price of our common stock may be highly volatile, and you may not be able to resell your shares at or above the price at which you purchased them.

Since our initial public offering, 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 $59.59 on September 21, 2018. 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 therapeutic candidates, including luspatercept, sotatercept, ACE-083 and ACE-2494;
- 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;
- actual or perceived changes in current or future 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.

We incur significant costs as a result of operating as a public company and complying with the Sarbanes-Oxley Act, and our management is required to devote substantial time to compliance initiatives. If we fail to maintain an effective system of

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internal control over financial reporting in the future, we may not be able to accurately report our financial condition, results of operations or cash flows, which may adversely affect investor confidence in us and, as a result, the value of our common stock.

As a public company, we incur significant legal, accounting and other expenses. In addition, the Sarbanes-Oxley Act, and rules of the SEC and those of Nasdaq have imposed various requirements on public companies including requiring establishment and maintenance of effective disclosure and financial controls. Our management and other personnel 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. We currently do not have an internal audit group, and we may need to hire additional accounting and financial staff with appropriate public company experience and technical accounting knowledge.

The Sarbanes-Oxley Act requires, among other things, that we maintain effective internal controls for financial reporting and disclosure controls and procedures. We are required, under Section 404 of the Sarbanes-Oxley Act, to furnish a report by management on, among other things, the effectiveness of our internal control over financial reporting. This assessment must include disclosure of any material weaknesses identified by our management in our internal control over financial reporting. A material weakness is a control deficiency, or combination of control deficiencies, in internal control over financial reporting that results in more than a reasonable possibility that a material misstatement of annual or interim financial statements will not be prevented or detected on a timely basis. In addition, we are required to have our independent registered public accounting firm attest to the effectiveness of our internal control over financial reporting.

During the evaluation and testing process, if we identify one or more material weaknesses in our internal control over financial reporting, we will be unable to assert that our internal control over financial reporting is effective. We cannot assure you that there will not be material weaknesses or significant deficiencies in our internal control over financial reporting in the future. Any failure to maintain internal control over financial reporting could severely inhibit our ability to accurately report our financial condition, results of operations or cash flows. If we are unable to conclude that our internal control over financial reporting is effective, or if our independent registered public accounting firm determines we have a material weakness or significant deficiency in our internal control over financial reporting, we could lose investor confidence in the accuracy and completeness of our financial reports, the market price of our common stock could decline, and we could be subject to sanctions or investigations by the Nasdaq, the SEC or other regulatory authorities. Failure to remedy any material weakness in our internal control over financial reporting, or to implement or maintain other effective control systems required of public companies, could also restrict our future access to 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, 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;
- 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;

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- 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, we are subject to the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a publicly-held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. As a result, you may lose your ability to sell your stock for a price in excess of the prevailing market price due to these protective measures and efforts by stockholders to change the direction or management of the company may be unsuccessful.

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.

Sales of our common stock by our employees, including our executive officers, could cause our stock price to fall or prevent it from increasing for numerous reasons, and sales by such persons could be viewed negatively by other investors.

In accordance with the guidelines specified under Rule 10b5-1 of the Securities Exchange Act of 1934, as amended, and our policies regarding stock transactions, a number of our employees, including executive officers, have adopted and may continue to adopt stock trading plans pursuant to which they have arranged to sell shares of our common stock from time to time in the future. Generally, sales under such plans by our executive officers and directors require

public filings. Sales of our common stock by such persons could cause the price of our common stock to fall or prevent it from increasing. If sales by employees, executive officers or directors cause a substantial number of shares of our common stock to become available for purchase in the public market, the price of our common stock could fall or may not increase. Also, sales by such persons could be viewed negatively by holders and potential purchasers of our common stock.

If securities analysts do not publish research or reports about our business or if they publish negative, or inaccurate, evaluations of our stock, the price of our stock and trading volume could decline.

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The trading market for our common stock may be impacted, in part, by the research and reports that securities or industry analysts publish about us or our business. There can be no assurance that analysts will cover us, continue to cover us or provide favorable coverage. If one or more analysts downgrade our stock or change their opinion of our stock, our share price may decline. In addition, if one or more analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our share price or trading volume to decline.

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Item 1B. Unresolved Staff Comments

Not applicable.

Item 2. Properties

Our corporate, research and development, manufacturing, and clinical trial operations are located in Cambridge, Massachusetts. We lease approximately 125,000 square feet of office and laboratory space in five adjacent buildings with aggregate monthly rent expense of approximately $0.5 million. Four of our leases expire in September 2023 and one lease expires in March 2021.

We believe our facilities are adequate for our current needs and that suitable additional substitute space would be available if needed.

Item 3. Legal Proceedings

While we are not currently a party to any material legal proceedings, we could become subject to legal proceedings in the ordinary course of business. We do not expect any such potential items to have a significant impact on our financial position.

Item 4. Mine Safety Disclosures

Not applicable.

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PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Market Information and Stockholders

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. As of January 31, 2019, there were approximately 61 holders of record of our common stock.

Dividends

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, 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.

Securities Authorized for Issuance Under Equity Compensation Plans

Information about our equity compensation plans is incorporated herein by reference to Item 12 of Part III of this Annual Report on Form 10-K.

Performance Graph

The following graph shows a comparison from September 19, 2013 through December 31, 2018 of cumulative total return on assumed investment of $100.00 in cash in our common stock, the Nasdaq Composite Index and the Nasdaq Biotechnology Index. Such returns are based on historical results and are not intended to suggest future performance. Data for the Nasdaq Composite Index and the Nasdaq Biotechnology Index assume reinvestment of dividends.

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COMPARISON OF 51 MONTH CUMULATIVE TOTAL RETURN(1)(2)
Among Acceleron Pharma Inc., the Nasdaq Composite Index, and the Nasdaq Biotechnology Index

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(1) This performance graph shall not be deemed "soliciting material" or to be "filed" with the SEC for purposes of Section 18 of the Securities and Exchange Act of 1934, as amended, or otherwise subject to the liabilities under that Section, and shall not be deemed incorporated by reference into any filing of Acceleron Pharma Inc. under the Securities Act of 1933, as amended.

(2) $100 invested on September 19, 2013 in stock, or on August 31, 2013 in each index, including reinvestment of dividends.

Purchases of Equity Securities by the Issuer or Affiliated Purchasers

None.

Item 6. 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 and with our consolidated financial statements and notes thereto included elsewhere in this Annual Report on Form 10-K. The selected financial data in this section is not intended to replace the consolidated financial statements and are qualified in their entirety by the consolidated financial statements and related notes included elsewhere in this Annual Report on Form 10-K.

The selected consolidated statements of operations data for the years ended December 31, 2018, 2017 and 2016 and the consolidated balance sheet data as of December 31, 2018 and 2017 have been derived from our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K. We derived the selected consolidated financial data for the years ended December 31, 2015 and 2014 and as of December 31, 2016, 2015 and 2014 from audited financial statements which are not included in this Annual Report on Form 10-K.

Historical results are not necessarily indicative of the results to be expected in future periods.

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	Year Ended December 31,				
(in thousands, except per share data)	2018	2017	2016	2015	2014
Consolidated Statements of Operations Data:					
Revenue:					
Collaboration revenue:					
License and milestone	$—	$541	$15,550	$1,184	$1,673
Cost-sharing, net	13,991	12,940	12,221	16,913	12,959
Total revenue	13,991	13,481	27,771	18,097	14,632
Costs and expenses:					
Research and development	103,902	89,726	68,580	58,404	50,897
Litigation settlement	—	—	—	—	5,000
General and administrative	34,503	33,738	25,297	20,572	14,199
Total costs and expenses	138,405	123,464	93,877	78,976	70,096
Loss from operations	(124,414)	(109,983)	(66,106)	(60,879)	(55,464)
Total other income (expense), net	5,516	1,561	9,116	(3,015)	4,205
Loss before income taxes	(118,898)	(108,422)	(56,990)	(63,894)	(51,259)
Income tax benefit (provision)	27	(32)	(24)	—	—
Net loss	$(118,871)	$(108,454)	$(57,014)	$(63,894)	$(51,259)
Net loss per share applicable to common stockholders-basic and diluted(1)	$(2.59)	$(2.68)	$(1.52)	$(1.92)	$(1.63)
Weighted-average number of common shares used in computing net loss per share applicable to common stockholders-basic and diluted	45,898	40,420	37,430	33,303	31,515

	As of December 31,				
(in thousands)	2018	2017	2016	2015	2014
Consolidated Balance Sheet Data:					
Cash and cash equivalents	$144,052	$100,150	$20,950	$27,783	$176,460
Short and long-term investments	147,260	272,800	213,432	108,198	—
Total assets	314,821	389,177	247,647	146,337	186,296
Total current liabilities	18,912	16,745	16,149	14,491	9,253
Long-term deferred revenue	—	3,161	3,704	4,239	4,816
Long-term deferred rent	2,381	1,818	953	1,157	1,818
Warrants to purchase common stock	1,491	2,236	1,244	17,187	14,124
Total stockholder's equity	292,037	365,217	225,597	109,263	156,285

(1) See Note 2 within the notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K for a description of the method used to calculate basic and diluted net loss per common share.

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Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

The following discussion of our financial condition and results of operations should be read in conjunction with our consolidated financial statements and the notes to those consolidated financial statements included in Item 15 of this Annual Report on Form 10-K. This discussion contains forward-looking statements that involve significant risks and uncertainties. As a result of many factors, such as those set forth under "Risk Factors" and elsewhere in this Annual Report on Form 10-K, our actual results may differ materially from those anticipated in these forward-looking statements. Please also refer to the section under heading "Forward-Looking Statements."

Overview

We are a leading biopharmaceutical company in the discovery and development of TGF-beta superfamily therapeutics to treat serious and rare diseases. Our research focuses on key natural regulators of cellular growth and repair, particularly the Transforming Growth Factor-Beta, or TGF-beta, protein superfamily. 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 generated several innovative therapeutic candidates, all of which encompass novel potential first-in-class mechanisms of action. We have focused and prioritized our research and development activities within three key therapeutic areas: hematologic, neuromuscular and pulmonary. If successful, these candidates could have the potential to significantly improve clinical outcomes for patients across these areas of high, unmet need.

Luspatercept, our lead program, and sotatercept, are partnered with Celgene Corporation, or Celgene. Luspatercept is an investigational erythroid maturation agent designed to promote red blood cell production through a novel mechanism, and is being developed to treat chronic anemia and associated complications in myelodysplastic syndromes, or MDS, beta-thalassemia, and myelofibrosis. In 2018, we and Celgene announced positive results for two Phase 3 clinical trials with luspatercept; one for the treatment of patients with lower-risk MDS with ring sideroblasts, known as the MEDALIST trial, and another for the treatment of patients with transfusion-dependent beta-thalassemia, also known as the BELIEVE trial. In the MEDALIST trial, luspatercept achieved a highly statistically significant improvement in the primary endpoint of red blood cell (RBC) transfusion independence of at least 8 consecutive weeks during the first 24 weeks compared to placebo. In the BELIEVE trial, luspatercept achieved a highly statistically significant improvement in the primary endpoint of erythroid response, which was defined as at least a 33 percent reduction from baseline in red blood cell (RBC) transfusion burden with a reduction of at least 2 units during the protocol-defined period of 12 consecutive weeks, from week 13 to week 24, compared to placebo. Results from the MEDALIST and BELIEVE trials were then presented during plenary and oral sessions, respectively, at the 60th American Society of Hematology Annual Meeting and Exposition in December 2018, and we expect to submit these results for publication during 2019. Both of these presentations were selected for "Best of ASH," chosen from among the thousands of meeting abstracts as "the biggest breakthroughs from the meeting's scientific presentations." We and Celgene are planning regulatory application submissions for luspatercept in both MDS and beta-thalassemia in the United States in April 2019 and in Europe in the first half of 2019.

In addition to the MEDALIST and BELIEVE Phase 3 clinical trials with luspatercept, Celgene is currently conducting a Phase 2 clinical trial in non-transfusion-dependent beta-thalassemia patients, referred to as the BEYOND trial, with preliminary top-line results currently expected in 2020. Celgene has also initiated a Phase 3 clinical trial, the COMMANDS trial, in first-line, lower-risk MDS patients and enrollment is ongoing. Enrollment is also currently ongoing in a Phase 2 clinical trial being conducted by Celgene for the treatment of patients with myelofibrosis, a rare bone marrow disorder, with preliminary top-line results currently expected in the second half of 2019. If luspatercept were to receive regulatory approval for each of these indications in the United States and Europe, we believe that there is an annual peak sales opportunity for luspatercept in excess of $2 billion across the indications in the BEYOND trial and the luspatercept Phase 3 clinical trials, and an annual peak sales opportunity for luspatercept in excess of $1 billion in myelofibrosis. We and Celgene are also evaluating further research of luspatercept for the treatment of anemia in potential new indications that could provide additional sales opportunities.

For sotatercept, we have the rights to fund, develop, and lead the global commercialization of sotatercept in pulmonary hypertension, which we refer to as the PH field, including pulmonary arterial hypertension, or PAH. PAH is a rare and chronic, rapidly progressing disorder characterized by the constriction of small pulmonary arteries,

resulting in abnormally high blood pressure in the pulmonary arteries. We are currently enrolling the PULSAR Phase 2 clinical trial of sotatercept for the treatment of patients with PAH with preliminary results expected in the first half of 2020, and we recently initiated an exploratory study, called SPECTRA, in the first quarter of 2019 to provide us with further understanding of sotatercept's impact on PAH. If sotatercept is commercialized to treat PAH and we recognize such revenue, then Celgene will be eligible to receive a royalty in the low 20% range on global net sales. In certain circumstances Celgene may recognize revenue related to the commercialization of sotatercept in PAH, and in this scenario we will be eligible to receive a royalty from Celgene such that the economic position of the parties is equivalent to the scenario in which we recognize such revenue.

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For luspatercept and, outside of the PH field, sotatercept, Celgene is responsible for paying 100% of the development costs for all clinical trials. We may receive a maximum of $545.0 million for the potential development, regulatory and commercial milestone payments. If luspatercept and, outside of the PH field, sotatercept are commercialized, we are eligible to receive a royalty on net sales in the low-to-mid 20% range. We have a co-promotion right in North America, for which our commercialization costs provided in the commercialization plan and budget as approved by the Joint Commercialization Committee will be entirely funded by Celgene, and from time to time we may elect to conduct additional activities to support commercialization of luspatercept at our own expense.

We are independently developing our wholly-owned neuromuscular candidate, ACE-083. ACE-083 is designed for the treatment of focal muscle disorders, and we are currently conducting Phase 2 clinical trials with ACE-083 in patients with facioscapulohumeral muscular dystrophy, or FSHD, as well as in patients with Charcot-Marie-Tooth disease, or CMT. We previously announced results from part 1 of each of our Phase 2 clinical trials in patients with FSHD and CMT showing increases in mean total and contractile muscle volume, reductions in fat fraction, and an encouraging safety profile. Enrollment is complete in part 2 of the ACE-083 Phase 2 clinical trial in patients with FSHD and is ongoing in the ACE-083 Phase 2 clinical trial in patients with CMT. We expect to announce preliminary results from part 2 of each of these Phase 2 clinical trials by the second half of 2019 for FSHD and by year end for CMT.

In addition to our mid- to late-stage clinical programs, we are currently conducting a Phase 1 healthy volunteer study with ACE-2494, our wholly-owned systemic muscle agent from our proprietary platform technology, IntelliTrap™, and we expect to report preliminary results from this healthy volunteer study in the first half of 2019. We are also conducting research primarily within our three focused disease areas—hematologic, neuromuscular and pulmonary—in order to identify new therapeutic candidates to advance into clinical trials.

As of December 31, 2018, our operations have been funded primarily by $105.1 million in equity investments from venture investors, $539.7 million from public investors, $123.7 million in equity investments from our collaboration partners and $284.2 million in upfront payments, milestones, and net research and development payments from our collaboration partners. We estimate that we have spent approximately $103.9 million, $89.7 million, and $68.6 million, on research and development for the years ended December 31, 2018, 2017, and 2016, respectively. On January 18, 2019, we completed the sale of 5,348,838 shares of common stock at a public offering price of $43.00 per share, resulting in net proceeds to us of approximately $215.8 million. In connection with the January 2019 public offering, on February 12, 2019, the underwriters fully exercised their option to purchase an additional 802,325 shares of our common stock. The total net proceeds to us from the January 2019 public offering and the underwriters' exercise of their option to purchase additional shares of our common stock was $248.2 million.

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 ACE-083, sotatercept, ACE-2494 or any future therapeutic candidates;
- continue our preclinical studies and potential clinical development efforts of our existing preclinical therapeutic candidates;
- continue research activities for the discovery of new therapeutic candidates;
- manufacture therapeutic candidates for our preclinical studies and clinical trials;
- acquire or in-license other therapeutic candidates and patents;
- seek regulatory approval for our therapeutic candidates; 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 therapeutic candidates. We expect that this will take a number of years and is subject to significant uncertainty. All current and future development and commercialization costs for luspatercept and, outside of pulmonary hypertension, sotatercept, as agreed to between us and Celgene are paid by Celgene. From time to time we may elect to conduct additional activities to support luspatercept at our own expense. If we obtain regulatory approval for ACE-083, sotatercept in the PH field, ACE-2494 or any future 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

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may have to significantly delay, scale back or discontinue the development or commercialization of one or more of our therapeutic candidates.

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 therapeutic candidates 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 therapeutic candidates. 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.

Costs and Expenses

Research and Development Expenses

Research and development expenses consist primarily of costs directly incurred by us for the development of our 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 therapeutic candidates or if, when, or to what extent we will generate revenues from the commercialization and sale of any of our 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 therapeutic candidates. The duration, costs and timing of clinical trials and development of 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.

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A change in the outcome of any of these variables with respect to the development of a therapeutic candidate could mean a significant change in the costs and timing associated with the development of that therapeutic candidate. For example, if the U.S. Food and Drug Administration, 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 therapeutic candidates, 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.

From inception through December 31, 2018, we have incurred $658.7 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-beta platform therapeutic candidates, the discovery and development of preclinical therapeutic candidates, and the development of our clinical programs. Research and development expenses associated with luspatercept, and outside of pulmonary hypertension, sotatercept, are generally reimbursed 100% by Celgene. These reimbursements are recorded as revenue. We are expensing the costs of a Phase 1 clinical trial for ACE-2494, and Phase 2 clinical trials for luspatercept, sotatercept, and ACE-083, of which the luspatercept clinical trials are reimbursed by Celgene. Our Phase 2 clinical trials for dalantercept have been discontinued.

We manage certain activities such as clinical trial operations, manufacture of therapeutic candidates, and preclinical animal toxicology studies through third-party CROs. The only costs we track by each therapeutic candidate are external costs such as services provided to us by CROs, manufacturing of preclinical and clinical drug product, 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, except for luspatercept costs for the purposes of billing Celgene. Our external research and development expenses during the years ended December 31, 2018, 2017 and 2016, were as follows:

	Year ended December 31,		
(in thousands)	2018	2017	2016
Luspatercept(1)	$6,518	$6,616	$6,945
Sotatercept(2)	8,633	495	—
Dalantercept(3)	—	4,718	6,757
ACE-083	11,778	9,797	4,973
ACE-2494	2,157	4,382	1,045
ACE-1334	2,064	—	—
Total direct research and development expenses	31,150	26,008	19,720
Other expenses(4)	72,752	63,718	48,860
Total research and development expenses	$103,902	$89,726	$68,580

(1) These expenses associated with luspatercept are reimbursed 100% by Celgene.

(2) These expenses are associated with our development of sotatercept in pulmonary arterial hypertension.

(3) Development of dalantercept has been discontinued.

(4) Other expenses include employee and unallocated contractor-related expenses, facility expenses, lab supplies and miscellaneous expenses.

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.

We continue to incur expenses related to audit, legal, regulatory and tax-related services associated with maintaining compliance with exchange listing and Securities and Exchange Commission, or SEC, 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 therapeutic candidates. Additionally, if and when we believe regulatory approval of a therapeutic candidate appears likely, to the extent that we are undertaking commercialization of such therapeutic

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candidate ourselves, we anticipate an increase in payroll and related expenses as a result of our preparation for commercial operation.

Other Income (Expense), Net

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

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 consolidated financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles. The preparation of these consolidated 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 consolidated 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 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 consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe the following accounting policies to be most critical to the judgments and estimates used in the preparation of our consolidated financial statements.

Revenue Recognition

Effective January 1, 2018, we adopted Accounting Standards Codification Topic 606, Revenue from Contracts with Customers, (ASC 606), using the modified retrospective transition method. Under this method, results for reporting periods beginning January 1, 2018 are presented under ASC 606, while prior period amounts are not adjusted and continue to be reported in accordance with ASC 605.

We have primarily generated revenue through collaboration, license and research arrangements, which are within the scope of ASC 606, with collaboration partners for the development and commercialization of therapeutic candidates. The arrangements generally contain performance obligations, which may include (1) licenses, or options to obtain licenses, to our technology, (2) research and development activities performed for the collaboration partners (3) participation on joint development committees (JDCs), and (4) the manufacturing of clinical or preclinical material. Payments pursuant to these arrangements typically include non-refundable, upfront payments, milestone payments upon achieving significant development events, research and development reimbursements, sales milestones, exercises of options, and royalties on future product sales.

Amounts received prior to satisfying the revenue recognition criteria are recorded as deferred revenue in our consolidated 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. 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. Amounts recognized as revenue, but not yet received or invoiced are generally recognized as contract assets, including collaboration receivables.

To determine revenue recognition for arrangements within the scope of ASC 606, we perform the following five steps: (i) identify the contract(s) with the customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation. We only apply the five-step model to contracts when it is probable that the entity will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of

ASC 606, we assess the goods or services promised within each contract, determines those that are performance obligations, and assesses whether each promised good or service is distinct. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied. Depending on the nature of the performance obligation these assessments require management to make significant judgments and estimates.

Exclusive Licenses

If the license to our intellectual property is determined to be distinct from the other promises or performance obligations identified in the arrangement, we recognize revenue from non-refundable, upfront fees allocated to the license when the license

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is transferred and the customer is able to use and benefit from the license. In order to assess whether the license is distinct, we consider the capabilities of the collaboration partner and the availability of the necessary expertise in the general marketplace to determine whether the collaboration partner can benefit from the license for its intended purpose without the receipt of the remaining elements. For licenses determined not to be distinct, we use judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. We evaluate the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition. The measure of progress, and thereby periods over which revenue should be recognized, are subject to estimates by management and may change over the course of the research and development and licensing agreement.

Research and Development Services

The promises under our collaboration and license agreements generally include research and development services to be performed by us on behalf of the collaboration partner. As the provision of research and development services is a part of our central operations, when we are principally responsible for the performance of these services under the agreements, we recognize revenue on a gross basis for research and development services in accordance with the ASC 606 framework described above.

Customer Options

Our agreements may contain options which provide the collaboration partner the right to obtain additional licenses. If an arrangement is determined to contain customer options, the goods and services underlying the customer options are not considered to be performance obligations at the inception of the arrangement, and the associated option fees are not included in the transaction price. We evaluate the customer options to determine if they represent material rights, which may include options to acquire additional goods or services for free or at a discount. If the customer options are determined to represent a material right, the material right is recognized as a separate performance obligation at the outset of the arrangement. We allocate the transaction price to material rights based on the relative standalone selling price, which is determined based on the identified discount and the probability that the customer will exercise the option. Amounts allocated to a material right are not recognized as revenue until, at the earliest, the option is exercised.

Milestone Payments

At the inception of each arrangement that includes milestone payments, we evaluate whether the milestones are considered probable of being achieved and estimates the amount to be included in the transaction price using the most likely amount method. We evaluate factors such as the scientific, clinical, regulatory, commercial, and other risks that must be overcome to achieve the respective milestone in making this assessment. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within our or our licensee's control, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. At the end of each subsequent reporting period, we reevaluate the probability of achievement of all milestones subject to constraint and, if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues and earnings in the period of adjustment. If a milestone or other variable consideration relates specifically to our efforts to satisfy a single performance obligation or to a specific outcome from satisfying the performance obligation, we generally allocate the milestone amount entirely to that performance obligation.

The next likely clinical milestone payment for luspatercept would be $25.0 million and result from U.S. Food and Drug Administration (FDA) or European Medicines Agency (EMA) acceptance of a Biologics Licensing Application

or equivalent for luspatercept in either myelodysplastic syndromes or beta-thalassemia. The Company and Celgene are planning regulatory application submissions for luspatercept in the United States in April 2019 and in Europe in the first half of 2019. Following application submission, the FDA will determine the acceptance of the application for "filing" by 60 days from the submission date. Similarly, the EMA will validate the application within 10 days of submission. In accordance with the Company's accounting policy regarding revenue recognition as described in Note 2, the revenue associated with this milestone will be recognized once it is probable that the applications are accepted for review by either the FDA or EMA. Milestone payments that are not within the control of the Company or the licensee are not considered probable of being achieved until those approvals are received. The acceptance of the application is not within the control of the Company or the licensee, and therefore, as of December 31, 2018, the Company cannot determine if it is probable that a regulatory agency will accept the application.

Royalties

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For arrangements that include sales-based royalties, including milestone payments based on a level of sales, and the license is deemed to be the predominant item to which the royalties relate, we recognize revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, we have not recognized any royalty revenue resulting from any of its licensing arrangements.

Accrued Clinical Trial Expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued expenses. This process involves reviewing contracts, and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost:

- CROs and investigative sites in connection with clinical studies;
- vendors in connection with preclinical development activities; and
- vendors related to product manufacturing, development and distribution of clinical supplies.

We base our expenses related to CROs and third-party service providers on our estimates of the services provided and efforts expended pursuant to quotes and contracts with CROs and third parties that conduct research and development on our behalf, as well as discussion with internal personnel and external service providers as to the progress of the services and the agreed-upon fee to be paid for such services. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense. We make significant judgments and estimates in determining the accrued balance in each reporting period. As actual costs become know, we adjust our accrued estimates. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed, the number of subjects enrolled, and the rate of enrollment may vary from its estimates and could result in us reporting amounts that are too high or too low in a particular period. Our accrued expenses are dependent, in part, upon the receipt of timely and accurate reporting from CROs and third-party service providers. To date, we have not experienced any material differences between accrued costs and actual costs incurred.

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, modifications to existing stock options, and restricted stock unit awards, 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. If achievement of the performance condition is not probable, but the award will vest based on the service condition, we recognize the expense over the requisite service period.

In July 2018, the Company early adopted ASU 2018-07, which expands the scope of Topic 718 to include share-based payments to non-employees. In connection with the adoption of this standard, the Company changed its accounting policy to establish the fair value of awards to non-employees at adoption date for existing awards and at grant date for new awards, rather than to mark such awards to market through the vesting period of the award. Additionally under the new guidance, the Company will use qualitative factors, such as exercise behavior and expected term to establish the term of the awards, rather than using contractual term, when valuing the awards. Forfeitures will be recognized as they occur.

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. We estimate our volatility by using a blend of our stock price history, for the length of time we have market data for our stock and the historical volatility of similar public companies for the expected term of each grant. 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 publicly traded companies. 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 have estimated the expected life of our employee stock options using the "simplified" method, whereby, the expected life equals the

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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.

Stock-based compensation totaled approximately $24.6 million, $28.2 million and $18.6 million for the years ended December 31, 2018, 2017 and 2016, respectively. 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.

Results of Operations

Comparison of the Years Ended December 31, 2018 and 2017

	Year Ended December 31,		Increase
(in thousands)	2018	2017	(Decrease)
Revenue:			
Collaboration revenue:			
License and milestone	$—	$541	$(541)
Cost-sharing, net	13,991	12,940	1,051
Total revenue (all amounts are with a related party)	13,991	13,481	510
Costs and expenses:			
Research and development	103,902	89,726	14,176
General and administrative	34,503	33,738	765
Total costs and expenses	138,405	123,464	14,941
Loss from operations	(124,414)	(109,983)	(14,431)
Other income, net	5,516	1,561	3,955
Loss before income taxes	(118,898)	(108,422)	(10,476)
Income tax provision	27	(32)	59
Net loss	$(118,871)	$(108,454)	$(10,417)

Revenue. We recognized revenue of $14.0 million in the year ended December 31, 2018, compared to $13.5 million in the year ended December 31, 2017. All of the revenue in both periods was derived from the Celgene agreements. Significant factors resulting in this $0.5 million increase include:

•an increase in cost-sharing revenue of $1.1 million primarily due to an increase in external expenses in preparation for the commercial launch of luspatercept; offset by

•a decrease in license and milestone revenue of $0.6 million resulting from the adoption of Accounting Standards Codification Topic 606, Revenue from Contracts with Customers, (ASC 606), the impact of which is discussed further in Note 2 to the financial statements in this Annual Report on Form 10-K.

Research and Development Expenses. Research and development expenses were $103.9 million in the year ended December 31, 2018, compared to $89.7 million in the year ended December 31, 2017. This $14.2 million increase is primarily related to growth in order to support our wholly-owned therapeutic candidates and preclinical programs and includes:

•an increase in personnel expenses totaling $7.3 million;

•an increase in external clinical trial expenses of $8.6 million related to our sotatercept and ACE-083 Phase 2 clinical trials;

•an increase in facility expenses of $1.9 million; offset by

•a decrease in toxicology expenses of $4.5 million as compared to the same period in 2017.

General and Administrative Expenses. General and administrative expenses were $34.5 million in the year ended December 31, 2018, compared to $33.7 million in the year ended December 31, 2017. The $0.8 million increase was primarily due to an increase in personnel expenses of $0.7 million related to increased headcount to support our growth.

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Other Income, Net. Other income, net was $5.5 million in the year ended December 31, 2018, compared to $1.6 million in the year ended December 31, 2017. This $3.9 million increase was primarily due to a $3.0 million increase in the interest earned on our investment portfolio as a result of our higher balance of interest-bearing cash equivalents and short- and long-term investments.

Income Tax Provision. Income tax provision is attributable to the realization of current year losses that offset unrealized gains, recognized in other comprehensive income, from our investment portfolio.

Comparison of the Years Ended December 31, 2017 and 2016

	Year Ended December 31,		Increase
(in thousands)	2017	2016	(Decrease)
Revenue:			
Collaboration revenue:			
License and milestone	$541	$15,550	$(15,009)
Cost-sharing, net	12,940	12,221	719
Total revenue (all amounts are with a related party)	13,481	27,771	(14,290)
Costs and expenses:			
Research and development	89,726	68,580	21,146
General and administrative	33,738	25,297	8,441
Total costs and expenses	123,464	93,877	29,587
Loss from operations	(109,983)	(66,106)	(43,877)
Other income, net	1,561	9,116	(7,555)
Loss before income taxes	(108,422)	(56,990)	(51,432)
Income tax provision	(32)	(24)	(8)
Net loss	$(108,454)	$(57,014)	$(51,440)

Revenue. We recognized revenue of $13.5 million in the year ended December 31, 2017, compared to $27.8 million in year ended December 31, 2016. All of the revenue in both periods was derived from the Celgene agreements. This $14.3 million decrease was primarily due to the receipt of a $15.0 million milestone payment from Celgene for the initiation of a Phase 3 clinical trial with luspatercept in 2016, offset in part by an increase in cost-sharing revenue of $0.7 million primarily related to an increase in reimbursement for personnel compared to the prior year.

Research and Development Expenses. Research and development expenses were $89.7 million in the year ended December 31, 2017, compared to $68.6 million in the year ended December 31, 2016. This $21.1 million increase was primarily due to increases in personnel expenses totaling $13.5 million to support development of our wholly-owned therapeutic candidates and preclinical programs, which includes an increase in stock-based compensation expense of $6.1 million. Other increases include clinical trial and toxicology expenses of $6.5 million and miscellaneous research and drug supply of $2.0 million. These increases were partially offset by a decrease in in-licensing expense related to payments that we made in connection with the achievement of a milestone in 2016 totaling $0.9 million.

General and Administrative Expenses. General and administrative expenses were $33.7 million in the year ended December 31, 2017, compared to $25.3 million in the year ended December 31, 2016. The $8.4 million increase was primarily due to an increase in personnel expenses of $8.7 million, which includes an increase in stock-based compensation expense of $3.6 million. The increase in stock-based compensation was primarily due to the modification of a former executive officer's equity awards announced in May 2017.

Other Income, Net. Other income, net was $1.6 million in the year ended December 31, 2017, compared to $9.1 million in the year ended December 31, 2016. This $7.5 million decrease was primarily due to an $8.3 million decrease in the gain associated with marking the common warrant liability to market, offset by an increase in interest income of $0.7 million.

Income Tax Provision. Income tax provision is attributable to taxes on interest income from our investment portfolio.

Liquidity and Capital Resources

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We have incurred losses and cumulative negative cash flows from operations since our inception in June 2003, and as of December 31, 2018, we had an accumulated deficit of $586.5 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 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 December 31, 2018, our operations have been primarily funded by $105.1 million in equity investments from venture investors prior to our IPO, $539.7 million from public investors, $123.7 million in equity investments from our partners and $284.2 million in upfront payments, milestones, and net research and development payments from our collaboration partners.

On January 11, 2016, we completed the sale of 3,750,000 shares of our common stock, at a public offering price of $40.00 per share, resulting in net proceeds to us of $140.4 million. On September 25, 2017, we completed the sale of 5,405,406 shares of our common stock at a public offering price of $37.00 per share. In connection with the September 2017 public offering, on October 4, 2017, the underwriters fully exercised their option to purchase an additional 810,810 shares of our common stock. The total net proceeds to us from the September 2017 public offering and the underwriters' exercise of their option to purchase additional shares of our common stock was $215.8 million.

On January 18, 2019, we completed the sale of 5,348,838 shares of our common stock, at a public offering price of $43.00 per share, resulting in net proceeds to us of $215.8 million. In connection with the January 2019 public offering, on February 12, 2019, the underwriters fully exercised their option to purchase an additional 802,325 shares of our common stock. The total net proceeds to us from the January 2019 public offering and the underwriters' exercise of their option to purchase additional shares of our common stock was $248.2 million.

As of December 31, 2018, we had $291.3 million in cash, cash equivalents and investments. Cash in excess of immediate requirements is invested in accordance with our investment policy, primarily with a view to liquidity and capital preservation.

Cash Flows

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

	Year Ended December 31,		
(in thousands)	2018	2017	2016
Net cash (used in) provided by:			
Operating activities	$(94,706)	$(76,544)	$(44,545)
Investing activities	122,927	(64,366)	(108,805)
Financing activities	16,146	220,296	146,667
Net increase (decrease) in cash and cash equivalents	$44,367	$79,386	$(6,683)

Operating Activities.

Net cash used in operating activities was $94.7 million for the year ended December 31, 2018, compared to $76.5 million and $44.5 million for the years ended December 31, 2017 and 2016, respectively. Net cash used in operating activities has increased over this three-year period as a result of increased headcount and related facilities as well as additional external expenses to support our wholly-owned therapeutic programs. The change primarily consists of our net losses adjusted for non-cash items and changes in components of operating assets and liabilities as follows:

•for the year ended December 31, 2018, a net loss of $118.9 million adjusted for non-cash items including: stock-based compensation expense of $24.6 million and depreciation and amortization expense of $3.7 million, and a net decrease of $4.6 million due to changes in operating assets and liabilities. The significant items in the change in operating assets and liabilities include an increase in prepaid expenses of $3.0 million primarily for start-up activities for the PULSAR clinical trial, and an increase in collaboration receivables of $3.5 million.

•for the year ended December 31, 2017, a net loss of $108.5 million adjusted for non-cash items including: stock-based compensation expense of $28.2 million, depreciation and amortization expense of $2.8 million and an increase in fair value of warrants of $1.0 million.

•for the year ended December 31, 2016, a net loss of $57.0 million adjusted for non-cash items including: stock-based compensation expense of $18.6 million, depreciation and amortization expense of $1.7 million, and a decrease in fair

value of warrants of $7.3 million.

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Investing Activities.

Net cash provided by investing activities was $122.9 million for the year ended December 31, 2018, compared to net cash used in investing activities of $64.4 million and $108.8 million for the years ended December 31, 2017 and 2016, respectively. Net cash provided by or used in, as applicable, investing activities primarily consisted of the following amounts relating to the activity within our investment portfolio:

•for the year ended December 31, 2018, net maturities of investments of $125.5 million;
•for the year ended December 31, 2017, net purchases of investments of $60.0 million; and
•for the year ended December 31, 2016, net purchases of investments of $105.4 million.

Net maturities for the year ended December 31, 2018 is the result of managing our investment portfolio to meet our projected cash requirements. Net purchases during the years ended December 31, 2017 and 2016 were due to the implementation of our investment policy when we began to invest the money raised in our September 2017 and January 2016 public offerings in marketable securities.

Financing Activities.

Net cash provided by financing activities was $16.1 million for the year ended December 31, 2018, compared to $220.3 million and $146.7 million for the years ended December 31, 2017 and 2016, respectively. Net cash provided by financing activities primarily consisted of net proceeds from our public offerings in 2017 and 2016, and, in all periods, cash proceeds from the exercise of stock options and issuance of common stock related to the employee stock purchase plan, as follows:

•for the year ended December 31, 2018, cash proceeds from the exercise of stock options and the issuance of common stock related to the employee stock purchase plan of $16.3 million;
•for the year ended December 31, 2017, net proceeds of $215.8 million from our September 2017 public offering and the underwriters full exercise of the over-allotment option in the offering, as well as $4.5 million in cash proceeds from the exercise of stock options and the issuance of common stock related to the employee stock purchase plan; and
•for the year ended December 31, 2016, net proceeds $140.7 million from our January 2016 public offering, as well as $6.0 million in cash proceeds from the exercise of stock options and the issuance of common stock related to the employee stock purchase plan.

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 therapeutic candidates. 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 ACE-083, sotatercept in pulmonary hypertension, ACE-2494 and any future therapeutic candidates, and begin to commercialize any approved products. We are subject to all of the risks incident in the development of therapeutic candidates, and we may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. 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.

Based on our current operating plan and projections, we believe that our current cash, cash equivalents and investments, together with the net proceeds from our January 2019 public offering, will be sufficient to fund our projected operating requirements until such time as we expect to receive significant royalty revenue from luspatercept sales. However, if there are changes in our operating plan or projections, we may need to raise additional funds for future development and operational plans and activities.

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, 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 therapeutic candidates. If we raise additional funds through the issuance of 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

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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 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 agreements 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 therapeutic candidates and potential therapeutic candidates;
- the number and characteristics of 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 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.

Contractual Obligations and Commitments

The following is a summary of our long-term contractual cash obligations as of December 31, 2018.

(in thousands)	Total	2019	2020 through 2021	2022 through 2023	After 2023
Operating lease obligations(1)	$39,402	$8,195	$16,618	$14,589	$ —
Less: sublease income(2)	(915)	(717)	(198)	—	—
Total	$38,487	$7,478	$16,420	$14,589	$ —

(1) We lease office and lab space at 128 Sidney Street, 149 Sidney Street, 99 Erie Street, and 167 Sidney Street in Cambridge, Massachusetts under noncancelable operating leases that expire in September 2023. We also lease office space at 125 Sidney Street under a noncancelable operating lease that expires in March 2021. Our leasehold improvements are being amortized over 4-7 years which represent the shorter of their useful life or remaining lease term. In accordance with the leases, the Company entered into cash-collateralized, irrevocable standby letters of

credit totaling $1.6 million, naming the respective landlords as beneficiaries.

(2) In July 2017, we entered into a sublease for 11,825 square feet of office and lab space at 99 Erie Street in Cambridge Massachusetts beginning on August 1, 2017. In January 2018 the subtenant exercised their right to extend the sublease through December 31, 2018. In December 2018, we entered into a new sublease agreement with a new

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subtenant, which commences upon the original subtenant vacating the facility. The new subtenant will pay rent on the lease through March 31, 2020.

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 consolidated 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 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 agreed to pay Salk specified development milestone payments totaling up to $2.0 million for sotatercept. Under the other agreement, we agreed to pay Salk specified development milestone payments of up to $0.7 million for luspatercept. 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 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.

- In May 2014, we executed a collaboration agreement with a research technology company. We paid an upfront and research fee of $0.3 million upon execution of the agreement. We also received an option to obtain a commercial license to the molecules developed during the collaboration, which, if exercised, would obligate us to pay royalty and milestone payments.

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.

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Net Operating Loss (NOL) Carryforwards

We have deferred tax assets of approximately $183.0 million as of December 31, 2018, 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, research and development tax credit carryforwards, and deferred revenue, accruals and other temporary differences. As of December 31, 2018, we had federal NOL carryforwards of approximately $556.0 million and state NOL carryforwards of $515 million available to reduce future taxable income, if any. Of these federal and state NOL carryforwards, $438.0 million and $515 million, respectively, will expire at various times through 2038. The federal NOL of $118.0 million generated in 2018 can be carried forward indefinitely. 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 our public offerings 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. For additional information about our taxes, see Note 13 to the financial statements in this Annual Report on Form 10-K.

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.

Item 7A. Quantitative and Qualitative Disclosures About Market Risks

We are exposed to market risk related to changes in interest rates. As of December 31, 2018 and December 31, 2017, we had cash, cash equivalents and investments of $291.3 million and $372.9 million, respectively. Our cash equivalents are invested primarily in bank deposits and money market mutual funds. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. Our investments are subject to interest rate risk and could fall in value if market interest rates increase. Due to the duration of our investment portfolio and the low risk profile of our investments, we do not believe an immediate 100 basis point change in interest rates would have a material effect on the fair market value of our portfolio. We have the ability to hold our investments until maturity, and therefore we would not expect our operating results or cash flows to be affected to any significant degree by the effect of a change in market interest rates on our investments.

Item 8. Financial Statements and Supplementary Data

All financial statements and supplementary data required to be filed hereunder are filed as listed under Item 15(a) of this Annual Report on Form 10-K and are incorporated herein by this reference.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

Item 9A. Controls and Procedures

Conclusion Regarding the Effectiveness of Disclosure Controls and Procedures

As of December 31, 2018, management, with the participation of our Chief Executive Officer and Chief Financial Officer, performed an evaluation of the effectiveness of the design and operation of our disclosure controls and procedures as defined in Rules 13a-15(e) and 15d-15(e) of the Exchange Act. Our disclosure controls and procedures are designed to ensure that information required to be disclosed in the reports we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission's rules and forms, and that such information is accumulated and communicated to our management, including the Chief Executive Officer and the Chief Financial Officer, to allow timely decisions regarding required disclosures. Any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objective. Based on this evaluation, our Chief Executive Officer and Chief Financial Officer concluded that, as of December 31, 2018, the design and operation of our disclosure controls and procedures were effective.

Management's Report on Internal Control Over Financial Reporting

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Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, is responsible for establishing and maintaining adequate internal control over financial reporting, as defined in Rule 13a-15(f) and 15d-15(f) of the Exchange Act. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policy or procedures may deteriorate. Under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, management has conducted an evaluation of the effectiveness of our internal control over financial reporting as of December 31, 2018 based upon the Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework). Based on this evaluation, management, including our Chief Executive Officer and Chief Financial Officer, has concluded that our internal control over financial reporting was effective as of December 31, 2018.
The effectiveness of our internal control over financial reporting as of December 31, 2018 has been audited by Ernst & Young LLP, our independent registered public accounting firm, as stated in their report which is included herein.
Changes in Internal Control over Financial Reporting
There were no changes in our internal control over financial reporting (as defined in Rule 13a-15(f) under the Exchange Act) during the quarter ended December 31, 2018, that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.
Report of Independent Registered Public Accounting Firm
To the Stockholders and the Board of Directors of Acceleron Pharma Inc.

Opinion on Internal Control over Financial Reporting

We have audited Acceleron Pharma Inc.’s internal control over financial reporting as of December 31, 2018, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). In our opinion, Acceleron Pharma Inc. (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2018, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of Acceleron Pharma Inc. as of December 31, 2018 and 2017, the related consolidated statements of operations and comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2018, and the related notes and our report dated February 27, 2019 expressed an unqualified opinion thereon.

Basis for Opinion

The Company’s management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management’s Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company’s internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects.

Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the

assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control Over Financial Reporting

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

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

/s/ Ernst & Young LLP
Boston, Massachusetts
February 27, 2019

Item 9B. Other Information

None.

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PART III

Item 10. Directors, Executive Officers and Corporate Governance

The information required by this Item 10 will be included in our definitive proxy statement to be filed with the Securities and Exchange Commission, or SEC, with respect to our 2019 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 11. Executive Compensation

The information required by this Item 11 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2019 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required by this Item 12 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2019 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 13. Certain Relationships and Related Transactions, and Director Independence

The information required by this Item 13 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2019 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services

The information required by this Item 14 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2019 Annual Meeting of Stockholders and is incorporated herein by reference.

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PART IV

Item 15. Exhibits and Financial Statement Schedules

(a) The following documents are filed as part of this report:

(1) Financial Statements.

(2) Financial Statement Schedules.

We are not filing any financial statement schedules as part of this Annual Report on Form 10-K because they are not applicable or the required information is included in the consolidated financial statements or notes thereto.

(3) Exhibits.

The list of Exhibits filed as a part of this Annual Report on Form 10-K is set forth on the Exhibit Index immediately preceding the signature page of this Annual Report on Form 10-K and is incorporated herein by this reference.

(b) The Exhibits filed or incorporated by reference as a part of this Annual Report on Form 10-K are set forth on the Exhibit Index immediately preceding the signature page of this Annual Report on Form 10-K.

(c) None.

Item 16. Form 10-K Summary

None.

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Acceleron Pharma Inc.
Index to Consolidated Financial Statements

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Report of Independent Registered Public Accounting Firm
To the Stockholders and the Board of Directors of Acceleron Pharma Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Acceleron Pharma Inc. (the Company) as of December 31, 2018 and 2017, the related consolidated statements of operations and comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2018, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2018 and 2017, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2018, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2018, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 Framework) and our report dated February 27, 2019 expressed an unqualified opinion thereon.

Adoption of New Accounting Standard

As discussed in Note 2 to the consolidated financial statements, the Company changed its method of accounting for revenue in 2018 due to the adoption of Accounting Standards Update (ASU) No. 2014-09, Revenue from Contracts with Customers (Topic 606), and related amendments.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the US federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2005.
Boston, Massachusetts
February 27, 2019

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Acceleron Pharma Inc.
Consolidated Balance Sheets
(amounts in thousands except share and per share data)

	December 31,	
	2018	2017
Assets		
Current assets:		
Cash and cash equivalents	$144,052	$100,150
Short-term investments	147,260	177,077
Collaboration receivables (all amounts are with a related party)	7,039	3,570
Prepaid expenses and other current assets	7,662	4,446
Total current assets	306,013	285,243
Property and equipment, net	7,106	6,966
Long-term investments	—	95,723
Restricted cash	1,597	1,132
Other assets	105	113
Total assets	$314,821	$389,177
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$419	$1,086
Accrued expenses	18,209	14,936
Deferred revenue	—	541
Deferred rent	284	182
Total current liabilities	18,912	16,745
Deferred revenue, net of current portion	—	3,161
Deferred rent, net of current portion	2,381	1,818
Warrants to purchase common stock	1,491	2,236
Total liabilities	22,784	23,960
Commitments and contingencies (Note 8)	—	—
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; 46,260,747 and 45,261,175 shares issued and outstanding at December 31, 2018 and 2017, respectively	47	46
Additional paid-in capital	879,099	839,090
Accumulated deficit	(586,549)	(473,024)
Accumulated other comprehensive loss	(560)	(895)
Total stockholders' equity	292,037	365,217
Total liabilities and stockholders' equity	$314,821	$389,177

See accompanying notes to consolidated financial statements.

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Acceleron Pharma Inc.
Consolidated Statements of Operations and Comprehensive Loss
(amounts in thousands except per share data)

	Year Ended December 31,		
	2018	2017	2016
Revenue:			
Collaboration revenue:			
License and milestone	$—	$541	$15,550
Cost-sharing, net	13,991	12,940	12,221
Total revenue (all amounts are with a related party)	13,991	13,481	27,771
Costs and expenses:			
Research and development	103,902	89,726	68,580
General and administrative	34,503	33,738	25,297
Total costs and expenses	138,405	123,464	93,877
Loss from operations	(124,414)	(109,983)	(66,106)
Other (expense) income, net	(52)	(992)	7,262
Interest income	5,568	2,553	1,854
Total other income, net	5,516	1,561	9,116
Loss before income taxes	(118,898)	(108,422)	(56,990)
Income tax benefit (provision)	27	(32)	(24)
Net loss	$(118,871)	$(108,454)	$(57,014)
Other comprehensive loss:			
Net unrealized holding gains (losses) on short- and long-term investments during the period net of tax of $95 thousand, zero, and zero for the years ended December 31, 2018, 2017, and 2016, respectively	335	(470)	(205)
Comprehensive loss	$(118,536)	$(108,924)	$(57,219)
Net loss per share- basic and diluted	$(2.59)	$(2.68)	$(1.52)
Weighted-average number of common shares used in computing net loss per share- basic and diluted	45,898	40,420	37,430

See accompanying notes to consolidated financial statements.

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Acceleron Pharma Inc.
Consolidated Statements of Stockholders' Equity
(amounts in thousands except share and per share data)

	Common Stock					
	Number of Shares	$0.001 Par Value	Additional Paid-In Capital	Accumulated Deficit	Comprehensive Loss	Total Stockholders' Equity
Balance at December 31, 2015	33,313,355	$ 34	$416,926	$ (307,477)	$ (220)	$ 109,263
Stock-based compensation	—	—	18,557	—	—	18,557
Issuance of common stock, net of expense $665	3,750,000	4	140,340	—	—	140,344
Exercise of stock options	885,075	1	5,311	—	—	5,312
Issuance of common stock related to ESPP	30,671	—	658	—	—	658
Net exercise of warrants to purchase common stock	272,725	—	8,682	—	—	8,682
Unrealized loss on available-for-sale securities	—	—	—	—	(205)	(205)
Net loss	—	—	—	(57,014)	—	(57,014)
Balance at December 31, 2016	38,251,826	39	590,474	(364,491)	(425)	225,597
Stock-based compensation	—	—	28,248	—	—	28,248
Issuance of common stock, net of expense $397	6,216,216	6	215,796	—	—	215,802
Exercise of stock options	474,056	1	3,892	—	—	3,893
Vesting of restricted stock units	282,158	—	(226)	—	—	(226)
Issuance of common stock related to ESPP	33,698	—	827	—	—	827
Net exercise of warrants to purchase common stock	3,221	—	—	—	—	—
Unrealized loss on available-for-sale securities	—	—	—	—	(470)	(470)
Effect of adoption of ASU 2016-09	—	—	79	(79)	—	—
Net loss	—	—	—	(108,454)		(108,454)
Balance at December 31, 2017	45,261,175	46	839,090	(473,024)	(895)	365,217
Stock-based compensation	—	—	24,569	—	—	24,569
Exercise of stock options	779,711	1	15,930	—	—	15,931
Vesting of restricted stock units	170,516	—	(731)	—	—	(731)
Issuance of common stock related to ESPP	30,896	—	1,085	—	—	1,085
Net exercise of warrants to purchase common stock	18,449	—	797	—	—	797
Unrealized loss on available-for-sale securities, net of tax	—	—	—	—	335	335
Effect of adoption of ASC 606	—	—	—	3,705	—	3,705
Effect of adoption of ASU 2018-07	—	—	(1,641)	1,641	—	—
Net loss	—	—	—	(118,871)	—	(118,871)
Balance at December 31, 2018	46,260,747	$ 47	$879,099	$ (586,549)	$ (560)	$ 292,037

See accompanying notes to consolidated financial statements.

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Acceleron Pharma Inc.
Consolidated Statements of Cash Flows
(amounts in thousands)

	Year Ended December 31,		
	2018	2017	2016
Operating Activities			
Net loss	$(118,871)	$(108,454)	$(57,014)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	3,747	2,825	1,676
Stock-based compensation	24,569	28,248	18,557
Change in fair value of warrants	52	992	(7,262)
Other non-cash items	357	176	(8)
Changes in assets and liabilities:			
Prepaid expenses and other current assets	(2,986)	(675)	(1,411)
Collaboration receivables (all amounts are with a related party)	(3,470)	(336)	394
Accounts payable	(673)	(504)	644
Accrued expenses	1,904	1,493	524
Deferred revenue	—	(543)	(549)
Deferred rent	665	234	(96)
Net cash used in operating activities	(94,706)	(76,544)	(44,545)
Investing Activities			
Purchase of investments	(73,570)	(179,935)	(218,314)
Proceeds from sales and maturities of investments	199,087	119,965	112,889
Purchases of property and equipment	(2,590)	(4,396)	(3,380)
Net cash provided by (used in) investing activities	122,927	(64,366)	(108,805)
Financing Activities			
Proceeds from issuance of common stock from public offering, net of issuance costs	—	215,802	140,697
Payments for withholding taxes on restricted stock units	(731)	(226)	—
Proceeds from issuances of common stock related to employee stock purchase plan	1,085	827	658
Proceeds from exercise of stock options and warrants to purchase common stock	15,931	3,893	5,312
Payments for capital lease expenditures	(139)	—	—
Net cash provided by financing activities	16,146	220,296	146,667
Net increase (decrease) in cash, cash equivalents and restricted cash	44,367	79,386	(6,683)
Cash, cash equivalents and restricted cash at beginning of year	101,282	21,896	28,579
Cash, cash equivalents and restricted cash at end of year	$145,649	$101,282	$21,896
Supplemental Disclosure of Non-Cash Investing and Financing Activities:			
Reclassification of warrant liability to additional paid-in capital	$797	$—	$8,682
Capitalized follow-on public offering costs included in accrued expenses	$221	$—	$—
Purchase of property and equipment included in accounts payable and accrued expenses	$1,159	$194	$397

See accompanying notes to consolidated financial statements.

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Acceleron Pharma Inc.
Notes to Consolidated Financial Statements
Years Ended December 31, 2018, 2017 and 2016

1. Nature of Business

Acceleron Pharma Inc. (Acceleron or the Company) is a Cambridge, Massachusetts-based clinical stage biopharmaceutical company dedicated to the discovery, development and commercialization of therapeutics to treat serious and rare diseases. The Company's leadership in the understanding of TGF-beta biology and protein engineering generates innovative compounds that engage the body's ability to regulate cellular growth and repair. The Company is subject to risks common to companies in the biotechnology industry, including, but not limited to, the risk that the Company never achieves profitability, the need for substantial additional financing, risk of relying on third parties, risks of clinical trial failures, dependence on key personnel, protection of proprietary technology and compliance with government regulations.

2. Summary of Significant Accounting Policies

The accompanying consolidated financial statements reflect the application of certain significant accounting policies as described below and elsewhere in these notes to the consolidated financial statements. The Company believes that a significant accounting policy is one that is both important to the portrayal of the Company's financial condition and results, and requires management's most difficult, subjective, or complex judgments, often as the result of the need to make estimates about the effect of matters that are inherently uncertain.

Principles of Consolidation

The accompanying consolidated financial statements include those of the Company and its wholly-owned subsidiary, Acceleron Securities Corp. All significant intercompany balances and transactions have been eliminated in consolidation.

Basis of Presentation

The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America (GAAP). Any reference in these notes to applicable guidance is meant to refer to the authoritative United States generally accepted accounting principles as found in the Accounting Standards Codification (ASC) and Accounting Standards Update (ASU) of the Financial Accounting Standards Board (FASB).

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the financial statements, and the reported amounts expensed during the reporting period.

Management considers many factors in selecting appropriate financial accounting policies and controls, and in developing the estimates and assumptions that are used in the preparation of these consolidated financial statements. Management must apply significant judgment in this process. In addition, other factors may affect estimates, including: expected business and operational changes, sensitivity and volatility associated with the assumptions used in developing estimates, and whether historical trends are expected to be representative of future trends. The estimation process often may yield a range of potentially reasonable estimates of the ultimate future outcomes and management must select an amount that falls within that range of reasonable estimates. This process may result in actual results differing materially from those estimated amounts used in the preparation of the consolidated financial statements if these results differ from historical experience, or other assumptions do not turn out to be substantially accurate, even if such assumptions are reasonable when made.

In preparing these consolidated financial statements, management used significant estimates in the following areas, among others: revenue recognition, stock-based compensation expense, the determination of the fair value of stock-based awards, the fair value of liability-classified warrants, accrued expenses, and the recoverability of the Company's net deferred tax assets and related valuation allowance.

Collaboration Receivable

Credit is extended to customers based upon an evaluation of the customer's financial condition. Collaboration receivables are recorded at net realizable value. The Company does not charge interest on past due balances. Collaboration receivables are

determined to be past due when the payment due date is exceeded. The Company utilizes a specific identification accounts receivable reserve methodology based on a review of outstanding balances and previous activities to determine the allowance for doubtful accounts. The Company charges off uncollectible receivables at the time the Company determines the receivable is no longer collectible. The Company did not have an allowance for doubtful accounts at December 31, 2018 or 2017.

Segment Information

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision maker, or decision making group, in making decisions on how to allocate resources and assess performance. The Company's chief operating decision maker is the chief executive officer. The Company and the chief executive officer view the Company's operations and manage its business as one operating segment, which is the discovery, development and commercialization of highly innovative therapeutics to treat serious and rare diseases. All material long-lived assets of the Company reside in the United States. The Company does use contract research organizations (CROs) and research institutions located outside the United States. Some of these expenses are subject to collaboration reimbursement which is presented as a component of cost-sharing, net in the consolidated statements of operations and comprehensive loss.

Cash, Cash Equivalents and Short-term and Long-term Investments

The Company considers all highly liquid investments purchased with original maturities of 90 days or less at the date of acquisition to be cash equivalents. Cash and cash equivalents include cash held in banks and amounts held in interest-bearing money market accounts, as well as marketable securities with a remaining maturity of 90 days or less. Cash equivalents are carried at cost, which approximates their fair market value.

The Company determines the appropriate classification of marketable securities at the time of purchase and reevaluates such designation at each balance sheet date. The Company has classified all of its marketable securities at December 31, 2018 and 2017 as “available-for-sale” pursuant to ASC 320, Investments – Debt and Equity Securities. The Company records available-for-sale securities at fair value, with the unrealized gains and losses included in accumulated other comprehensive income (loss) in stockholders’ equity. There were no realized gains or losses on marketable securities for the years ended December 31, 2018, 2017 and 2016.

Investments not classified as cash equivalents are presented as either short-term or long-term investments based on both their maturities as well as the time period the Company intends to hold such securities.

The Company adjusts the cost of available-for-sale debt securities for amortization of premiums and accretion of discounts to maturity. The Company includes such amortization and accretion in interest income. The cost of securities sold is based on the specific identification method. The Company includes interest and dividends on securities classified as available-for-sale in interest income in the accompanying consolidated statements of operations and comprehensive loss.

The Company reviews marketable securities for other-than-temporary impairment whenever the fair value of a marketable security is less than the amortized cost and evidence indicates that a marketable security’s carrying amount is not recoverable within a reasonable period of time. Other-than-temporary impairments of investments are recognized in the consolidated statements of operations if the Company has experienced a credit loss, has the intent to sell the marketable security, or if it is more likely than not that the Company will be required to sell the marketable security before recovery of the amortized cost basis. Evidence considered in this assessment includes reasons for the impairment, compliance with the Company’s investment policy, the severity and the duration of the impairment and changes in value subsequent to the end of the period.

The aggregate fair value of securities held by the Company in an unrealized loss position for less than twelve months as of December 31, 2018 and December 31, 2017 was $51.2 million and $193.6 million, respectively. The aggregate fair value of securities held by the Company in an unrealized loss position for more than twelve months as of December 31, 2018 and December 31, 2017 was $94.3 million and $67.0 million, respectively. The aggregate

unrealized loss for those securities in an unrealized loss position for more than twelve months was $0.4 million and $0.3 million, respectively. The Company evaluated its securities for other-than-temporary impairment and considered the decline in market value for the securities to be primarily attributable to current economic and market conditions. It is not more likely than not that the Company will be required to sell the securities, and the Company does not intend to do so prior to the recovery of the amortized cost basis. Based on this analysis, these marketable securities were not considered to be other-than-temporarily impaired as of December 31, 2018 and December 31, 2017.

Concentrations of Credit Risk and Off-Balance Sheet Risk

The Company has no off-balance sheet risk, such as foreign exchange contracts, option contracts, or other foreign hedging arrangements. Financial instruments that potentially subject the Company to concentrations of credit risk are primarily cash, cash equivalents, restricted cash, short-term and long-term investments and collaboration receivables. The Company maintains its cash and cash equivalent balances and short-term and long-term investments with financial institutions that management believes are creditworthy. Short-term and long-term investments consist of investment grade corporate obligations, treasury notes, asset backed securities, and certificates of deposit. The Company's investment policy includes guidelines on the quality of the institutions and financial instruments and defines allowable investments that the Company believes minimizes the exposure to concentrations of credit risk. The Company routinely assesses the creditworthiness of its customers and collaboration partners. The Company has not experienced any material losses related to receivables from individual customers and collaboration partners, or groups of customers. The Company does not require collateral. Due to these factors, no additional credit risk beyond amounts provided for collection losses is believed by management to be probable in the Company's collaboration receivables.

Disclosure of Fair Value of Financial Instruments

The Company's financial instruments include cash, cash equivalents, short-term and long-term investments, collaboration receivables, common stock warrants, accounts payable, and accrued expenses. See discussion below on the determination of the fair value of the Company's common stock warrants and short-term and long-term investments. The carrying value of the remainder of the Company's financial instruments approximated their fair values at December 31, 2018 and 2017 due to the short-term nature of these instruments. The Company has evaluated the estimated fair value of financial instruments using available market information and management's estimates. The use of different market assumptions and/or estimation methodologies could have a significant effect on the estimated fair value amounts.

Fair Value Measurements

ASC Topic 820, Fair Value Measurement (ASC 820), establishes a fair value hierarchy for instruments measured at fair value that distinguishes between assumptions based on market data (observable inputs) and the Company's own assumptions (unobservable inputs). Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's assumptions about the inputs that market participants would use in pricing the asset or liability, and are developed based on the best information available in the circumstances.

ASC 820 identifies fair value as the exchange price, or exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As a basis for considering market participant assumptions in fair value measurements, ASC 820 establishes a three-tier fair value hierarchy that distinguishes between the following:

- Level 1—Quoted market prices in active markets for identical assets or liabilities.
- Level 2—Inputs other than Level 1 inputs that are either directly or indirectly observable, such as quoted market prices, interest rates, and yield curves.
- Level 3—Unobservable inputs developed using estimates of assumptions developed by the Company, which reflect those that a market participant would use.

To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

Items measured at fair value on a recurring basis include short-term and long-term investments (Note 5), and warrants to purchase common stock (Note 7). During the periods presented, the Company has not changed the manner in which

it values assets and liabilities that are measured at fair value using Level 3 inputs.

The following tables set forth the Company's financial instruments carried at fair value using the lowest level of input applicable to each financial instrument as of December 31, 2018 and 2017 (in thousands):

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Acceleron Pharma Inc.
Notes to Consolidated Financial Statements (Continued)
Years Ended December 31, 2018, 2017 and 2016

	December 31, 2018			
	Quoted Prices in Active Markets for Identical Items (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Total
Assets:				
Money market funds	$74,023	$ —	$ —	$74,023
Corporate obligations	—	128,920	—	128,920
U.S. Treasury securities	—	56,978	—	56,978
Certificates of deposit	—	1,715	—	1,715
Mortgage and other asset backed securities	—	26,874	—	26,874
Restricted cash	1,597	—	—	1,597
Total assets	$75,620	$ 214,487	$ —	$290,107
Liabilities:				
Warrants to purchase common stock	$—	$ —	$ 1,491	$1,491
Total liabilities	$—	$ —	$ 1,491	$1,491

	December 31, 2017			
	Quoted Prices in Active Markets for Identical Items (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Total
Assets:				
Money market funds	$90,702	$—	$ —	$90,702
Corporate obligations	—	158,849	—	158,849
U.S. Treasury securities	—	37,813	—	37,813
Certificates of deposit	—	12,244	—	12,244
Mortgage and other asset backed securities	—	67,888	—	67,888
Restricted cash	1,132	—	—	1,132
Total assets	$91,834	$ 276,794	$ —	$368,628
Liabilities:				
Warrants to purchase common stock	$—	$ —	$ 2,236	$2,236
Total liabilities	$—	$ —	$ 2,236	$2,236

The money market funds noted above are included in cash and cash equivalents in the accompanying consolidated balance sheets. The Company recognizes transfers between levels of the fair value hierarchy as of the end of the reporting period. There were no transfers within the hierarchy during the years ended December 31, 2018 and 2017. The following table sets forth a summary of changes in the fair value of the Company's common stock warrant liabilities, which represent a recurring measurement that is classified within Level 3 of the fair value hierarchy, wherein fair value is estimated using significant unobservable inputs (in thousands):

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Acceleron Pharma Inc.
Notes to Consolidated Financial Statements (Continued)
Years Ended December 31, 2018, 2017 and 2016

	Year Ended December 31,	
	2018	2017
Beginning balance	$2,236	$1,244
Change in fair value	52	992
Exercises	(797)	—
Ending balance	$1,491	$2,236

The fair value of the warrants to purchase common stock on the date of issuance and on each re-measurement date for those warrants classified as liabilities was estimated using either the Monte Carlo simulation framework, which incorporates future financing events over the remaining life of the warrants to purchase common stock, or for certain re-measurement dates, due to the warrants being deeply in the money, the Black-Scholes option pricing model. The Black-Scholes method of valuation involves using inputs such as the fair value of the Company's stock, stock price volatility, the contractual term of the warrants, risk-free interest rates, and dividend yields. At each reporting period the Company evaluates the best valuation methodology. At December 31, 2018, and December 31, 2017 the Black-Scholes option pricing model was used, and at December 31, 2016, the Monte Carlo simulation framework was used. Due to the nature of these inputs, the valuation of the warrants is considered a Level 3 measurement.

See Note 7 for further discussions of the accounting for the warrants, as well as for a summary of the significant inputs and assumptions used to determine the fair value of the warrants.

The Company measures eligible assets and liabilities at fair value, with changes in value recognized in earnings. Fair value treatment may be elected either upon initial recognition of an eligible asset or liability or, for an existing asset or liability, if an event triggers a new basis of accounting. The Company did not elect to remeasure any of its existing financial assets or liabilities, and did not elect the fair value option for any financial assets and liabilities transacted in the years ended December 31, 2018 or 2017.

Property and Equipment

Property and equipment is stated at cost. Maintenance and repairs that do not improve or extend the lives of the respective assets are expensed to operations as incurred. Upon disposal, retirement or sale the related cost and accumulated depreciation is removed from the accounts and any resulting gain or loss is included in the results of operations. Depreciation and amortization is calculated using the straight-line method over the estimated useful lives of the assets, which are as follows:

Asset	Estimated Useful Life
Computer equipment and software	3 years
Office and laboratory equipment	3 years
Leasehold improvements	Shorter of the useful life or remaining lease term

The Company reviews long-lived assets when events or changes in circumstances indicate the carrying value of the assets may not be recoverable. Recoverability is measured by comparison of the book values of the assets to future net undiscounted cash flows that the assets are expected to generate. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount by which the book value of the assets exceed their fair value, which is measured based on the projected discounted future net cash flows arising from the assets. No impairment losses have been recorded during the years ended December 31, 2018, 2017 and 2016.

Accrued Clinical Trial Expenses

The Company accrues for estimated costs of research and development activities conducted by third-party service providers, which includes the conduct of clinical trials. The Company records the estimated costs of clinical trial activities based upon the estimated amount of services provided and includes the costs incurred but not yet invoiced within accrued liabilities on the balance sheet and within research and development expense in the consolidated statements of operations and comprehensive loss. These costs can be a significant component of the Company's

research and development expenses.

The Company estimates the amount of services provided and efforts expended pursuant to quotes and contracts with third parties, as well as discussion with internal personnel and external service providers as to the progress of the services and the

agreed-upon fee to be paid for such services. The Company makes significant judgments and estimates in determining the accrued balance in each reporting period. As actual costs become known, it adjusts its accrued estimates. Although the Company does not expect its estimates to be materially different from amounts actually incurred, its understanding of the status and timing of services performed, the number of subjects enrolled, and the rate of enrollment may vary from its estimates and could result in the Company reporting amounts that are too high or too low in a particular period. The Company's accrued expenses are dependent, in part, upon the receipt of timely and accurate reporting from contract research organizations and third-party service providers. To date, the Company has not experienced any material differences between accrued costs and actual costs incurred.

Revenue Recognition

Effective January 1, 2018, the Company adopted Accounting Standards Codification Topic 606, Revenue from Contracts with Customers, (ASC 606), using the modified retrospective transition method. Under this method, results for reporting periods beginning January 1, 2018 are presented under ASC 606, while prior period amounts are not adjusted and continue to be reported in accordance with ASC 605.

The Company has primarily generated revenue through collaboration, license and research arrangements, which are within the scope of ASC 606, with collaboration partners for the development and commercialization of therapeutic candidates. The arrangements generally contain performance obligations, which may include (1) licenses, or options to obtain licenses, to the Company's technology, (2) research and development activities performed for the collaboration partners (3) participation on joint development committees (JDCs), and (4) the manufacturing of clinical or preclinical material. Payments pursuant to these arrangements typically include non-refundable, upfront payments, milestone payments upon achieving significant development events, research and development reimbursements, sales milestones, exercises of options, and royalties on future product sales.

Amounts received prior to satisfying the revenue recognition criteria are recorded as deferred revenue in the Company's consolidated 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. 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. Amounts recognized as revenue, but not yet received or invoiced are generally recognized as contract assets, including collaboration receivables.

To determine revenue recognition for arrangements within the scope of ASC 606, the Company performs the following five steps: (i) identify the contract(s) with the customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation. The Company only applies the five-step model to contracts when it is probable that the entity will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, the Company assesses the goods or services promised within each contract, determines those that are performance obligations, and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied. Depending on the nature of the performance obligation these assessments require management to make significant judgments and estimates.

Exclusive Licenses

If the license to the Company's intellectual property is determined to be distinct from the other promises or performance obligations identified in the arrangement, the Company recognizes revenue from non-refundable, upfront fees allocated to the license when the license is transferred and the customer is able to use and benefit from the license. In order to assess whether the license is distinct, the Company considers the capabilities of the collaboration partner and the availability of the necessary expertise in the general marketplace to determine whether the collaboration partner can benefit from the license for its intended purpose without the receipt of the remaining elements. For licenses determined not to be distinct the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition. The measure of progress, and thereby periods over which revenue should be recognized, are subject to estimates by management and may change over the course of the research and development and licensing agreement.

Research and Development Services

The promises under the Company’s collaboration and license agreements generally include research and development services to be performed by the Company on behalf of the collaboration partner. As the provision of research and development services is a part of the Company’s central operations, when the Company is principally responsible for the performance of these services under the agreements, the Company recognizes revenue on a gross basis for research and development services in accordance with the ASC 606 framework described above.

Customer Options

The Company's agreements may contain options which provide the collaboration partner the right to obtain additional licenses. If an arrangement is determined to contain customer options, the goods and services underlying the customer options are not considered to be performance obligations at the inception of the arrangement, and the associated option fees are not included in the transaction price. The Company evaluates the customer options to determine if they represent material rights, which may include options to acquire additional goods or services for free or at a discount. If the customer options are determined to represent a material right, the material right is recognized as a separate performance obligation at the outset of the arrangement. The Company allocates the transaction price to material rights based on the relative standalone selling price, which is determined based on the identified discount and the probability that the customer will exercise the option. Amounts allocated to a material right are not recognized as revenue until, at the earliest, the option is exercised.

Milestone Payments

At the inception of each arrangement that includes milestone payments, the Company evaluates whether the milestones are considered probable of being achieved and estimates the amount to be included in the transaction price using the most likely amount method. The Company evaluates factors such as the scientific, clinical, regulatory, commercial, and other risks that must be overcome to achieve the respective milestone in making this assessment. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the control of the Company or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. At the end of each subsequent reporting period, the Company reevaluates the probability of achievement of all milestones subject to constraint and, if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues and earnings in the period of adjustment. If a milestone or other variable consideration relates specifically to the Company's efforts to satisfy a single performance obligation or to a specific outcome from satisfying the performance obligation, the Company generally allocates the milestone amount entirely to that performance obligation.

Royalties

For arrangements that include sales-based royalties, including milestone payments based on a level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, the Company has not recognized any royalty revenue resulting from any of its licensing arrangements.
Research and Development Expenses

Research and development costs are charged to expense as costs are incurred in performing research and development activities. Research and development costs include all direct costs, including salaries, stock compensation and benefits for research and development personnel, outside consultants, costs of clinical trials, sponsored research, clinical trials insurance, other outside costs, depreciation and facility costs related to the development of drug candidates. The Company records upfront, non-refundable payments made to outside vendors, or other payments made in advance of services performed or goods being delivered, as prepaid expenses, which are expensed as services are performed or the goods are delivered.

Certain research and development projects are, or have been, partially funded by collaboration agreements, and the expenses related to these activities are included in research and development costs. The Company records the related reimbursement of research and development costs under these agreements as revenue, as more fully described above and in Note 10.

Stock-Based Compensation

At December 31, 2018, the Company had two stock-based compensation plans, which are more fully described in Note 11. The Company accounts for stock-based compensation in accordance with the provisions of ASC Topic 718, Compensation—Stock Compensation (ASC 718), which requires the recognition of expense related to the fair value of stock-based compensation awards in the consolidated statements of operations and comprehensive loss.

For stock-based awards issued to employees and members of the Company's board of directors (the Board) for their services on the Board and for participation in the employee stock purchase plan, the Company estimates the grant date fair value of each option award using the Black-Scholes option pricing model. The use of the Black-Scholes option pricing model requires management to make assumptions with respect to the expected term of the option, the expected volatility of the common stock consistent with the expected life of the option, risk-free interest rates and expected dividend yields of the common stock. For awards subject to service-based vesting conditions, the Company recognizes stock-based compensation expense, equal to the grant date fair value of stock options on a straight-line basis over the requisite service period, which is generally the vesting term. For awards subject to both performance and service-based vesting conditions, the Company recognizes stock-based compensation expense using an accelerated recognition method when it is probable that the performance condition will be achieved. If achievement of the performance condition is not probable, but the award will vest based on the service condition, expense is recognized over the requisite service period.

In July 2018, the Company early adopted ASU 2018-07, which expands the scope of Topic 718 to include share-based payments to non-employees. In connection with the adoption of this standard, the Company changed its accounting policy to establish the fair value of awards to non-employees at adoption date for existing awards and at grant date for new awards, rather than to mark such awards to market through the vesting period of the award. Additionally under the new guidance, the Company will use qualitative factors, such as exercise behavior and expected term to establish the term of the awards, rather than using contractual term, when valuing the awards. Forfeitures will be recognized as they occur. Upon adoption, a cumulative adjustment of $1.6 million was booked to increase retained earnings for the impact to the Company's outstanding awards to non-employees. The provisions of the standard were adopted prospectively and prior periods were not retrospectively adjusted.

See Note 11 for a discussion of the assumptions used by the Company in determining the grant date fair value of options granted under the Black-Scholes option pricing model, as well as a summary of the stock option activity under the Company's stock-based compensation plans for the year ended December 31, 2018.

Income Taxes

Income taxes are recorded in accordance with ASC Topic 740, Income Taxes (ASC 740), which provides for deferred taxes using an asset and liability approach. The Company recognizes deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements or tax returns. Deferred tax assets and liabilities are determined based on the difference between the financial statement and tax bases of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Valuation allowances are provided, if based upon the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized.

The Company accounts for uncertain tax positions in accordance with the provisions of ASC 740. When uncertain tax positions exist, the Company recognizes the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position as well as consideration of the available facts and circumstances. As of December 31, 2018 or 2017, the Company does not have any significant uncertain tax positions.

Net Loss Per Share

The Company calculates basic and diluted net loss per common share by dividing the net loss by the weighted-average number of common shares outstanding during the period. For the years ended December 31, 2018, 2017 and 2016, the

Company has excluded the effects of all potentially dilutive shares, which include outstanding common stock options, warrants to purchase common stock, common stock issuable under the employee stock purchase plan, and restricted stock units, from the weighted-average number of common shares outstanding as their inclusion in the computation for these years would be anti-dilutive due to net losses incurred.

The following is a summary of the common stock equivalents which were excluded from the calculation of diluted net loss per share for the periods indicated (in thousands):

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	Year Ended December 31,		
	2018	2017	2016
Outstanding stock options	3,513	3,452	3,316
Common stock warrants	39	61	64
Shares issuable under employee stock purchase plan	18	18	23
Restricted stock units	608	604	732
Total excluded common stock equivalents	4,178	4,135	4,135

Comprehensive Loss

Comprehensive loss is defined as the change in equity of a business enterprise during a period from transactions, other events, and circumstances from non-owner sources. Comprehensive loss consists of net loss and other comprehensive loss, which includes certain changes in equity that are excluded from net loss. Comprehensive loss has been disclosed in the accompanying consolidated statements of operations and comprehensive loss. Accumulated other comprehensive loss is presented separately on the consolidated balance sheets and consists entirely of unrealized holdings losses on investments as of December 31, 2018 and 2017.

Subsequent Events

The Company considers events or transactions that occur after the balance sheet date but prior to the issuance of the financial statements to provide additional evidence relative to certain estimates or to identify matters that require additional disclosure. Subsequent events have been evaluated as required. The Company has evaluated all subsequent events and determined that there are no material recognized or unrecognized subsequent events requiring disclosure, other than the January 2019 public offering of common stock as discussed in Note 9 and elsewhere in this Annual Report on Form 10-K.

Recent Accounting Pronouncements - Not Yet Adopted

From time to time, new accounting pronouncements are issued by the FASB or other standard setting bodies and adopted by the Company as of the specified effective date. Unless otherwise discussed, the Company believes that the impact of recently issued standards that are not yet effective will not have a material impact on its financial position or results of operations upon adoption.

In February 2016, the FASB issued ASU 2016-02, Leases (Topic 842), Amendments to the FASB Accounting Standards Codification, which replaces the existing guidance for leases. ASU 2016-02 requires the identification of arrangements that should be accounted for as leases by lessees. In general, for lease arrangements exceeding a twelve month term, these arrangements must now be recognized as assets and liabilities on the balance sheet of the lessee. Under ASU 2016-02, a right-of-use asset and lease obligation will be recorded for all leases, whether operating or financing, while the income statement will reflect lease expense for operating leases and amortization/interest expense for financing leases. The balance sheet amount recorded for existing leases at the date of adoption of ASU 2016-02 must be calculated using the applicable incremental borrowing rate at the date of adoption.

ASU 2016-02 is effective for annual and interim periods beginning after December 15, 2018 and requires modified retrospective method in which the new guidance is applied on the date of the initial application. In July 2018, the FASB issued ASU 2018-11, Leases - Targeted Improvements, intended to ease the implementation of the new lease standard for financial statement preparers by, among other things, allowing for an additional transition method. In lieu of presenting transition requirements to comparative periods, as previously required, an entity may now elect to show a cumulative effect adjustment on the date of adoption without the requirement to recast prior financial statements or disclosures presented in accordance with ASU 2016-02. The Company expects to adopt the new standard and elect to use the cumulative effect adjustment transition option effective January 1, 2019, which will be the initial date of

application.

The Company currently expects to elect the available package of practical expedients which allows the Company to not reassess previous accounting conclusions around whether arrangements are or contain leases, the classification of leases, and the treatment of initial direct costs. The Company also expects it will make an accounting policy election to keep leases with an initial term of 12 months or less off of the balance sheet. The Company is continuing to assess the impact that adopting the new standard and its amendments will have on its consolidated financial statements and related disclosures.

In preparation for adoption of the standard, the Company is in the process of implementing internal controls to enable the preparation of financial information including the assessment of the impact of the standard. The adoption of the new standard is expected to result in the recognition of additional lease liabilities and right-of-use assets as of January 1, 2019 which will have a material impact to the Company's consolidated balance sheets.

3. Property and Equipment, Net

Property and equipment, net, consists of the following (in thousands):

	December 31,	
	2018	2017
Computer equipment and software	$1,712	$1,501
Office equipment	672	522
Laboratory equipment	19,948	17,268
Leasehold improvements	11,668	11,501
Construction in progress	1,139	584
Total property and equipment	35,139	31,376
Accumulated depreciation and amortization	(28,033)	(24,410)
Property and equipment, net	$7,106	$6,966

Depreciation and amortization expense was $3.7 million, $2.8 million and $1.7 million for the years ending December 31, 2018, 2017 and 2016, respectively.

4. Restricted Cash

On January 1, 2018, the Company adopted ASU 2016-18, Statement of Cash Flows - Restricted Cash (Topic 230). This new standard requires companies to include amounts generally described as restricted cash and restricted cash equivalents in cash and cash equivalents when reconciling beginning-of-period and end-of-period total amounts shown on the statement of cash flows. As a result of the adoption, there was no impact to cash flows from investing or financing activities for the year ended December 31, 2018, 2017, and 2016. The $1.1 million of restricted cash related to collateral for the Company's facility lease obligation and its credit cards, which was previously reported as an adjustment to net loss in cash flows used in operating activities for the year ended December 31, 2017 and 2016 is no longer presented within the net change in cash, cash equivalents and restricted cash, as it is considered part of cash, cash equivalents and restricted cash.

The following table provides a reconciliation of cash, cash equivalents and restricted cash reported within the consolidated balance sheet that sum to the total of the same such amounts shown in the statement of cash flows (in thousands):

	December 31,		
	2018	2017	2016
Cash and cash equivalents	$144,052	$100,150	$20,950
Restricted cash	1,597	1,132	946
Total cash, cash equivalents and restricted cash shown in the statement of cash flows	145,649	101,282	21,896

As of December 31, 2018, 2017, and 2016, the Company maintained letters of credit totaling $1.6 million, $1.1 million and $0.9 million, respectively, held in the form of certificates of deposit as collateral for the Company's facility lease obligations and its credit cards.

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5. Cash, Cash Equivalents and Short-term and Long-term Investments

The following is a summary of cash, cash equivalents and available-for-sale securities as of December 31, 2018 and December 31, 2017 (in thousands):

	December 31, 2018			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Cash and cash equivalents due in 90 days or less	$144,064	$ —	$ (12)	$144,052
Available-for-sale securities:				
Corporate obligations due in one year or less	73,671	—	(267)	73,404
U.S. Treasury securities due in one year or less	45,346	—	(79)	45,267
Certificates of deposit due in one year or less	1,715	—	—	1,715
Mortgage and other asset backed securities due in one year or less	26,982	—	(108)	26,874
Total available-for-sale securities	$147,714	$ —	$ (454)	$147,260
Total cash, cash equivalents and available-for-sale securities	$291,778	$ —	$ (466)	$291,312

	December 31, 2017			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Cash and cash equivalents due in 90 days or less	$100,150	$ —	$ —	$100,150
Available-for-sale securities:				
Corporate obligations due in one year or less	99,792	—	(219)	99,573
Corporate obligations due in more than one year	57,537	—	(261)	57,276
U.S. Treasury securities due in one year or less	27,987	—	(93)	27,894
U.S. Treasury securities due in more than one year	9,968	—	(48)	9,920
Certificates of deposit due in one year or less	10,529	—	—	10,529
Certificates of deposit due in more than one year	1,715	—	—	1,715
Mortgage and other asset backed securities due in one year or less	39,236	—	(155)	39,081
Mortgage and other asset backed securities due in more than one year	26,931	—	(119)	26,812
Total available-for-sale securities	$273,695	$ —	$ (895)	$272,800
Total cash, cash equivalents and available-for-sale securities	$373,845	$ —	$ (895)	$372,950

6. Accrued Expenses

Accrued expenses consist of the following (in thousands):

	December 31,	
	2018	2017
Research and development related	$8,144	$4,014
Employee compensation	7,975	6,809
Professional services	621	1,183
Accrued purchases	351	150
Other	1,118	2,780
Total accrued expenses	$18,209	$14,936

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7. Warrants

Below is a summary of the number of shares issuable upon exercise of outstanding warrants and the terms and accounting treatment for the outstanding warrants (in thousands, except per share data):

	Warrants as of		Weighted-Average Exercise		Balance Sheet Classification	
	December 31, 2018	December 31, 2017	Price Per Share	Expiration	December 31, 2018	December 31, 2017
Warrants to purchase common stock	39	61	$ 5.88	June 10, 2020 - July 9, 2020	Liability (1)	Liability (1)
All warrants	39	61	$ 5.88			

(1) In January 2018, the warrant holders exercised warrants to purchase 21,258 shares of Common Stock on a net basis, resulting in the issuance of 18,449 shares of Common Stock.

Upon issuance the Company concluded the anti-dilution feature required the warrants to be classified as liabilities under ASC Topic 815, Derivatives and Hedging—Contracts in Entity's Own Equity (ASC 815). The warrants are measured at fair value, with changes in fair value recognized as a gain or loss to other income (expense) in the consolidated statements of operations and comprehensive loss for each reporting period thereafter. The fair value of the common stock warrants was recorded as a discount to the preferred stock issued, and the preferred stock was accreted to the redemption value. At the end of each reporting period, the Company remeasured the fair value of the outstanding warrants, using current assumptions, resulting in an increase (decrease) in fair value of $0.1 million, $1.0 million and $(7.3) million, respectively, which was recorded in other income (expense), net in the accompanying consolidated statements of operations and comprehensive loss for the years ended December 31, 2018, 2017 and 2016. The Company will continue to re-measure the fair value of the liability associated with the warrants to purchase common stock at the end of each reporting period until the earlier of the exercise or the expiration of the applicable warrants. All outstanding warrants were fully vested and exercisable as of December 31, 2018.

8. Commitments and Contingencies

Operating Leases

The Company leases its facilities under non-cancelable operating leases that expire at various dates through September 2023. All of the Company's leases contain escalating rent clauses, which require higher rent payments in future years. The Company expenses rent on a straight-line basis over the term of the lease, including any rent-free periods. In addition, the Company received certain lease incentives, and recorded these incentives as deferred rent, which is amortized as a reduction of rent expense over the life of the lease. Rent expense of approximately $5.8 million, $4.8 million and $3.8 million were incurred during the years ended December 31, 2018, 2017 and 2016, respectively.

Future annual minimum lease payments as of December 31, 2018, are as follows (in thousands):

2019	$8,195
2020	8,438
2021	8,180
2022	8,256
2023	6,333
Total	$39,402

In July 2017, the Company entered into a sublease for 11,825 square feet of office and lab space at 99 Erie Street in Cambridge Massachusetts beginning on August 1, 2017. In January 2018 the subtenant exercised their right to extend the sublease through December 31, 2018. In December 2018, the Company entered into a new sublease agreement with a new subtenant, which commences upon the original subtenant vacating the facility. The new subtenant will pay rent on the lease through March 31, 2020. Sublease income of approximately $0.7 million, $0.3 million, and zero was recorded during the years ended December 31, 2018, 2017 and 2016, respectively. Future annual minimum sublease proceeds expected as of December 31, 2018 are as follows (in thousands):

2019	$717
2020	198
Total	$915

Legal Proceedings

The Company, from time to time, may be party to litigation arising in the ordinary course of its business. Except as discussed below, the Company was not subject to any material legal proceedings during the years ended December 31, 2018, 2017 and 2016, and, to the best of its knowledge, no material legal proceedings are currently pending or threatened.

Other

The Company is also party to various agreements, principally relating to licensed technology, that require future payments relating to milestones not met at December 31, 2018 and 2017, or royalties on future sales of specified products. No milestone or royalty payments under these agreements are expected to be payable in the immediate future. See Note 10 for discussion of these arrangements.

The Company enters into standard indemnification agreements in the ordinary course of business. Pursuant to the agreements, the Company indemnifies, holds harmless, and agrees to reimburse the indemnified party for losses suffered or incurred by the indemnified party, generally the Company's business partners or customers, in connection with any U.S. patent or any copyright or other intellectual property infringement claim by any third party with respect to the Company's products. The term of these indemnification agreements is generally perpetual any time after execution of the agreement. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is unlimited. The Company has never incurred costs to defend lawsuits or settle claims related to these indemnification agreements.

9. Stockholders' Equity

On January 11, 2016, the Company completed the sale of 3,750,000 shares of common stock at a public offering price of $40.00 per share, resulting in net proceeds to the Company of approximately $140.3 million.

On September 25, 2017, the Company completed the sale of 5,405,406 shares of common stock at a public offering price of $37.00 per share. On October 4, 2017, in connection with the September 2017 public offering, the underwriters fully exercised their option to purchase an additional 810,810 shares of common stock. The total net proceeds to the Company from the September 2017 public offering and the underwriters' exercise of their option to purchase additional shares of common stock was $215.8 million.

On January 18, 2019, the Company completed the sale of 5,348,838 shares of common stock at a public offering price of $43.00 per share, resulting in net proceeds to the Company of approximately $215.8 million. In connection with the January 2019 public offering, on February 12, 2019, the underwriters fully exercised their option to purchase an additional 802,325 shares of common stock. The total net proceeds to the Company from the January 2019 public offering and the underwriters' exercise of their option to purchase additional shares of common stock was $248.2 million.

Preferred Stock

The Company’s certificate of incorporation authorizes the Board to issue up to 25,000,000 shares of preferred stock from time to time in one or more series. The rights, preferences, restrictions, qualifications and limitations of such stock are determined by the Board. As of December 31, 2018 no shares are issued or outstanding.

Common Stock

The holders of shares of common stock are entitled to one vote for each share of common stock held at all meetings of stockholders and written actions in lieu of meetings.

The holders of shares of common stock are entitled to receive dividends, if and when declared by the Board. No dividends have been declared or paid by the Company through December 31, 2018.

Common Stock Reserved for Future Issuance

At December 31, 2018, the Company has reserved for future issuance the following number of shares of common stock (in thousands):

	December 31, 2018
Outstanding stock options to purchase common stock	3,513
Outstanding restricted stock units	608
Shares available for future issuance under equity incentive plan	3,556
Warrants to purchase common stock	39
Shares available for future issuance under the employee stock purchase plan	156
Additional shares reserved for unissued, but designated, Preferred Stock	25,000
Total shares of authorized common stock reserved for future issuance	32,872

10. Significant Agreements

Celgene

Overview

On February 20, 2008 the Company entered into an agreement with Celgene relating to sotatercept (the Original Sotatercept Agreement), which was amended on August 2, 2011 (as amended, the Amended Sotatercept Agreement). The Company further amended and restated the Original Sotatercept Agreement in its entirety on September 18, 2017, (the Restated Sotatercept Agreement). On August 2, 2011 the Company entered into a second agreement with Celgene for luspatercept, (the Luspatercept Agreement).

Restated Sotatercept Agreement

The Restated Sotatercept Agreement provides Celgene with an exclusive license to sotatercept outside of the field of pulmonary hypertension, referred to as the PH field, and provides the Company with the worldwide rights to develop and commercialize sotatercept in the PH field.

In connection with the Restated Sotatercept Agreement, Celgene agreed not to develop or commercialize in PH field any compound developed under the Restated Sotatercept Agreement or the Luspatercept Agreement, and the Company agreed not to develop or commercialize any compound developed under the Restated Sotatercept Agreement or the Luspatercept Agreement in any field outside the PH field. The Company has the right to license, transfer or sell its rights to develop and commercialize sotatercept in the PH field, subject to Celgene's right of first negotiation.

The Company is responsible for 100% of the costs related to its development and commercialization of sotatercept in the PH field. If sotatercept is commercialized to treat pulmonary hypertension and the Company recognizes such revenue, then Celgene will be eligible to receive a royalty in the low 20% range on global net sales. In certain circumstances Celgene may recognize revenue related to the commercialization of sotatercept in the PH field, and in this scenario, the Company will be eligible to receive a royalty from Celgene such that the economic position of the parties is equivalent to the scenario in which the Company recognizes such revenue. With respect to the development and commercialization of sotatercept outside of the PH field or the development and commercialization of any other compound under the Restated Sotatercept Agreement, the terms of the Amended Sotatercept Agreement, described below, remained unchanged.

Pursuant to the Restated Sotatercept Agreement, Celgene will provide the Company with certain quantities of Celgene's existing clinical supply of sotatercept for development in the PH field at no cost. For clinical or commercial supply of sotatercept in excess of that which is agreed to under the Restated Sotatercept Agreement, Celgene can elect to provide the Company with such clinical and commercial supply of sotatercept at a negotiated price or provide a tech transfer to enable the Company to manufacture on its own behalf. The conduct of the collaboration is managed by a Joint Development Committee and Joint Commercialization Committee. In the event of a deadlock of a committee,

the Company shall determine the resolution of issues specifically related to the PH field, (other than pricing which shall be determined by consensus), and Celgene shall determine the resolution of all other issues. The Joint Commercialization Committee will oversee

commercialization of sotatercept, and sotatercept pricing will be determined by mutual agreement of the Company and Celgene in the Joint Commercialization Committee.

The Restated Sotatercept Agreement will expire on a country-by-country basis on the occurrence of the latest to occur of the following: (1) the expiration of the royalty term with respect to all license products outside the PH field in such country, (2) the expiration of the royalty term with respect to all sotatercept licensed products in the PH field in such country, and (3) the exercise or forfeiture by Celgene of its option with regard to each option compound. In the PH field, the royalty term for each licensed product in each country is the period commencing with first commercial sale of the applicable licensed product in the applicable country and ending on the latest of expiration of specified patent coverage or a specified period of years. Outside the PH field, the royalty term for each licensed product in each country outside North America is the period commencing with first commercial sale of the applicable licensed product in the applicable country and ending on the latest of expiration of specified patent coverage or a specified period of years, and the royalty term for each licensed product in North America is the period commencing with the first commercial sale in North America and ending, on a licensed product and country-by-country basis on the date which commercialization of such licensed product has ceased. The term for each option compound runs for a specified period of years unless Celgene exercises its option, in which case the compound becomes a licensed product, or forfeits its option by failing to make certain payments following the achievement of certain milestones in early clinical development of the option compound.

The Restated Sotatercept Agreement is 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 Restated Sotatercept 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 the Company or termination by Celgene for convenience or failure to meet an endpoint will have the effect of terminating the applicable license to Celgene and the rights granted to the Company with respect to the development of sotatercept in the PH field shall become irrevocable. Termination for cause by either party shall result in reducing the remaining royalties due to the breaching party by a certain percentage. Upon termination by Celgene for convenience or for failure to meet an endpoint, the Company and Celgene will enter into a termination agreement pursuant to which, among other things, Celgene will continue to be eligible to receive a royalty in the low 20% range on global net sales of sotatercept in the PH field.

The Company was not required to make any upfront payments to Celgene upon execution of the Restated Sotatercept Agreement, and is not be required to make any milestone payments to Celgene in connection with its development and commercialization of sotatercept in the PH field.

Original and Amended Sotatercept Agreement

Under the Original Sotatercept Agreement, as preserved by the Amended Sotatercept Agreement, the Company granted Celgene an exclusive license to sotatercept in all indications and an option to license discovery stage compounds against three specified targets. Celgene paid $45.0 million of nonrefundable, upfront license and option payments to the Company and bought $5.0 million of equity upon closing in February 2008. Per the Original Sotatercept Agreement, concurrent with the Company's 2013 IPO, Celgene purchased an additional $10.0 million of the Company's common stock.

The Company retained responsibility for research and development of sotatercept through the end of Phase 2a clinical trials, as well as manufacturing the clinical supplies for these trials. These activities were substantially completed in 2011. Celgene will be responsible for any sotatercept Phase 3 clinical trials, as well as any additional Phase 2 clinical trials and is responsible for manufacturing or overseeing the manufacture of Phase 3 and commercial supplies.

Commensurate with the execution of the Luspatercept Agreement described below, in August 2011 the Company and Celgene agreed to modify the terms of the collaboration. Outside of the PH field, the significant financial terms of the Amended Sotatercept Agreement, which were preserved in the Restated Sotatercept Agreement, are:

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Since January 1, 2013, Celgene has been responsible for paying 100% of worldwide development costs for the sotatercept program;

- Celgene will be responsible for all commercialization costs worldwide as agreed in the budget between the Company and Celgene;
- The Company will be eligible to receive tiered royalty payments in the low-to-mid 20% percent range on net sales of sotatercept subject to certain reductions, including for entry of a generic product onto the market; and
- The Company is obligated to co-promote sotatercept and future products in all fields, in each case if approved, in North America, and Celgene will pay all costs related thereto;

The Amended Sotatercept Agreement, as preserved in the Restated Sotatercept Agreement, contains a two-category contingent development milestone structure outside of the PH field (oncology and non-oncology) for sotatercept, including future clinical milestones of up to $27.0 million, regulatory milestones of up to $190.0 million and commercial milestones of up to $150.0 million. Additionally, the Company is eligible to receive option fees of up to $30.0 million for each of the three discovery-stage targets, and for all three discovery-stage targets in the aggregate, clinical milestones of up to $25.5 million, regulatory milestones of up to $142.5 million and commercial milestones of up to $150.0 million. None of the three discovery stage programs has advanced to the stage to achieve payment of a milestone, nor does the Company expect any such milestone payments in the near future.

As of December 31, 2018, the Company has received $44.5 million in research and development funding and milestone payments for the sotatercept program. The next likely clinical milestone payment would be $10.0 million and result from Celgene's start of a Phase 3 study with sotatercept outside of the PH field.

Luspatercept Agreement

Under the terms of the Luspatercept Agreement, the Company and Celgene collaborate worldwide for the joint development and commercialization of luspatercept. The Company also granted Celgene an option for future products for which Acceleron files an Investigational New Drug application for the treatment of anemia. Celgene paid $25.0 million on the closing of the Luspatercept Agreement in August 2011.

The Company retained responsibility for research and development through the end of Phase 1 and the Company's initial luspatercept beta-thalassemia and luspatercept MDS Phase 2 clinical trials, as well as manufacturing the clinical supplies for these studies. Celgene will conduct subsequent Phase 2 and Phase 3 clinical studies and will be responsible for overseeing the manufacture of Phase 3 and commercial supplies by third party contract manufacturing organizations. The significant financial terms of the Luspatercept Agreement are:

- Since January 1, 2013, Celgene has been responsible for paying 100% of worldwide development costs for the luspatercept program;
- Celgene will be responsible for all commercialization costs worldwide as agreed in the budget between the Company and Celgene;
- The Company will be eligible to receive tiered royalty payments in the low-to-mid 20% percent range on net sales of luspatercept subject to certain reductions, including for entry of a generic product onto the market; and
- The Company is obligated to co-promote luspatercept and future products in all fields, in each case if approved, in North America, and Celgene will pay all costs related thereto;

Additionally, from time to time the Company may elect to conduct additional activities to support luspatercept at its own expense. The Company is eligible to receive clinical milestones of up to $32.5 million, regulatory milestones of up to $105.0 million and commercial milestones of up to $80.0 million for luspatercept. The Company will receive additional, lower development, regulatory, and commercial milestones for any additional products for the treatment of anemia on which Celgene exercises an option.

The Luspatercept Agreement will expire on a country-by-country basis on the occurrence of both of the following: (1) the expiration of the royalty term with respect to all license products in such country, and (2) the end of the option term. The royalty term for each licensed product in each country outside North America is the period commencing with first commercial sale of the applicable licensed product in the applicable country and ending on the latest of expiration of specified patent coverage or a specified period of years. The royalty term for each licensed product in North America is the period commencing with the first commercial sale in North America and ending, on a licensed product and country-by-country basis on the date which commercialization of such licensed product has ceased. The option term runs until the later of (1) the date on which no development or commercialization activities are ongoing or are expected to commence for any licensed products under the Luspatercept Agreement; (2) the date on which no development or commercialization activities are ongoing or are expected to commence for any licensed products

under the Restated Sotatercept Agreement and all option rights under the Restated Sotatercept Agreement have been forfeited with respect to each option compound where Celgene has made a payment with respect to such compound; and (3) the royalty term for all licensed products under the Luspatercept Agreement and the Restated Sotatercept Agreement has ended; provided that if at the time the option term would otherwise end any option compounds under the Luspatercept Agreement are in clinical development the option term shall continue until Celgene's rights to such compound are either exercised or forfeited.

Celgene has the right to terminate the Luspatercept Agreement with respect to one or more licensed targets or in its entirety, upon 180 days' notice (or 45 days' notice if the licensed product has failed to meet certain end point criteria with respect to clinical trials or other development activities). The agreement may also be terminated in its entirety by either Celgene or the Company in the event of a material breach by the other party or in the event of a bankruptcy filing of the other party. There are no cancellation, termination or refund provisions in this arrangement that contain material financial consequences to the Company.

Through December 31, 2018, the Company has received $109.6 million in research and development funding and milestone payments for luspatercept. The next likely clinical milestone payment would be $25.0 million and result from the U.S. Food and Drug Administration or European Medical Association acceptance of a Biologics Licensing Application or equivalent for luspatercept in either myelodysplastic syndromes or beta-thalassemia. The Company has not yet identified additional compounds for the treatment of anemia so there is no assurance that the Company will generate future value from additional products.

Accounting Analysis

The Company accounted for the Restated Sotatercept Agreement and Luspatercept Agreement ander ASC 606, effective January 1, 2018. The Company identified the following material promises under the Restated Sotatercept Agreement and Luspatercept Agreement: (1) licenses to develop and commercialize sotatercept and luspatercept; (2) performance of research and development services; (3) participation in the JDCs; and (4) the performance of the manufacturing services. The Company determined that the licenses to sotatercept and luspatercept technology, the research and development activities, participation in the JDCs and the manufacturing services are each distinct performance obligations. The option rights to future products related to the treatment of anemia under the Luspatercept Agreement are not considered to represent a material right as this right is a protective provision akin to exclusivity and does not represent a customer option to receive the rights or services at a discount. In addition, the Company is under no obligation to discover, develop, or deliver any new compounds that modulate anemia. Therefore, the option right under the Luspatercept Agreement is not a performance obligation. Commercialization support for each of sotatercept and luspatercept is considered to be a participatory right and not a performance obligation. The Company concluded that services provided for the extension studies do not represent a contract modification or a performance obligation but rather a separate services arrangement, which is accounted for as a separate contract. Each study includes one promise, the completion of the study, which is distinct from the performance obligations in the Restated Sotatercept Agreement and Luspatercept Agreement that is satisfied over time, and the consideration for each study approximates the stand-alone selling price. Revenue is recognized as the services for each study are provided.

The most significant change in the Company’s accounting policy relates to the recognition of milestone revenue. Prior to January 1, 2018, the Company recognized revenue in accordance with ASC 605, Revenue Recognition. At the inception of each arrangement that included milestone payments, the Company evaluated, with respect to each milestone, whether the milestone was substantive and at-risk. The Company evaluated 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 achievement date, assuming all other revenue recognition criteria are met and the milestone is deemed substantive and at-risk, the Company recognized the payment as license and milestone revenue. For milestones that were not deemed substantive and at-risk, where payment was reasonably assured, the Company recognized the milestone payment over the remaining service period.

Under ASC 606, future potential milestone payments were excluded from the transaction price as they are still subject to completion of on-going clinical studies or other risks that are outside of the Company's control and therefore the risk of significant reversal has not been resolved. The next likely clinical milestone payment for luspatercept would be $25.0 million and result from U.S. Food and Drug Administration (FDA) or European Medicines Agency (EMA) acceptance of a Biologics Licensing Application or equivalent for luspatercept in either myelodysplastic syndromes or beta-thalassemia. The Company and Celgene are planning regulatory application submissions for luspatercept in the United States in April 2019 and in Europe in the first half of 2019. Following application submission, the FDA will determine the acceptance of the application for "filing" by 60 days from the submission date. Similarly, the EMA will validate the application within 10 days of submission. In accordance with the Company's accounting policy regarding revenue recognition as described in Note 2, the revenue associated with this milestone will be recognized once it is probable that the applications are accepted for review by either the FDA or EMA. Milestone payments that are not within the control of the Company or the licensee are not considered probable of being achieved until those approvals are received. The acceptance of the application is not within the control of the Company

or the licensee, and therefore, as of December 31, 2018, the Company cannot determine if it is probable that a regulatory agency will accept the application.

The transaction price includes the following payments received under the Restated Sotatercept and Luspatercept Agreement through the adoption date of December 31, 2017 for a total of $192.3 million, as follows:

- $25.0 million upfront fee in connection with the closing of the Luspatercept Agreement;
- $45.0 million of nonrefundable, upfront license and option payments in connection with the closing of the Original and Amended Sotatercept Agreements;
- $14.9 million received for sotatercept development and manufacturing activities;
- $47.9 million received for luspatercept development and manufacturing activities; and
- $59.5 million milestone payments pursuant to the agreements.

The Company allocated the total transaction price to the identified performance obligations (both satisfied and unsatisfied) using the estimated standalone selling price of each performance obligation as of the adoption date of ASC 606. The Company’s estimate of the standalone selling price requires judgment, in particular in estimating the value of the license rights for luspatercept and sotatercept, which includes assumptions over the projected revenues and expenses, probability of technical and regulatory success and appropriate discount rates.

As of the ASC 606 adoption date, the only remaining undelivered element is participation in the JDC for which there was a deferred revenue balance of $3.7 million. The transaction price allocated to participation in the JDC based on the established standalone selling price of all performance obligations was de minimis as the sotatercept and luspatercept licenses carried the most significant portion of the value included in the agreements, and the Company's remaining effort on the JDC is minimal.

As a result of adopting ASC 606 on January 1, 2018, the Company has recorded a cumulative-effect reduction to opening accumulated deficit of $3.7 million as of January 1, 2018 and a corresponding decrease to deferred revenue, of which $0.5 million was recorded to current deferred revenue and $3.2 million was recorded to long-term deferred revenue. License and milestone revenue for the year ended December 31, 2018 was zero, as compared to the $0.5 million that would have been recorded under ASC 605. Deferred revenue as of December 31, 2018 was zero under ASC 606, as compared to a balance of $3.2 million, which would have resulted under ASC 605.

Through December 31, 2018, under all Celgene arrangements the Company has received net cost-share payments and milestones of $109.6 million and $44.5 million for luspatercept and sotatercept, respectively. The Company recorded net cost-sharing revenue of $14.0 million, $12.9 million, and $12.2 million during the years ended December 31, 2018, 2017, and 2016, respectively.

Other Agreements

Other

In 2004, the Company entered into a license agreement with a non-profit institution for an exclusive, sublicensable, worldwide, royalty-bearing license to certain patents developed by the institution (Primary Licensed Products). In addition, the Company was granted a non-exclusive, non-sub-licensable license for Secondary Licensed Products. As

compensation for the licenses, the Company issued 62,500 shares of its common stock to the institution, the fair value of which was $25,000, and was expensed during 2004, to research and development expense. The Company also agreed to pay specified development milestone payments totaling up to $2.0 million for sotatercept and $0.7 million for luspatercept. In addition, the Company is obligated to pay milestone fees based on the Company's research and development progress, and U.S. sublicensing revenue ranging from 10%-25%, as well as a royalty ranging from 1.0%-3.5% of net sales on any products developed under the licenses. During the years ended December 31, 2018, 2017 and 2016, the Company paid and expensed milestones and fees defined under the agreement totaling $0.1 million, $0.1 million and $0.1 million, respectively, which is recorded as research and development expense.

In May 2014, the Company executed a collaboration agreement with a research technology company. The Company paid an upfront and research fee of $0.3 million upon execution of the agreement and the Company is obligated to pay additional research fees of approximately $0.6 million over approximately the next year, depending on the success of the research program. The Company also received an option to obtain a commercial license to the molecules developed during the collaboration. During the years ended December 31, 2018, 2017, and 2016, the Company expensed milestones and fees totaling $0.1 million, $1.6 million, and $1.0 million, which is recorded as research and development expense.

11. Stock-Based Compensation

At December 31, 2018, the Company had two stock-based compensations plans, which are more fully described below.

The Company's 2003 Stock Option and Restricted Stock Plan (the 2003 Plan) provided for the issuance of stock options and restricted stock to employees, officers, directors, consultants and key personnel of the Company as determined by the Board. In conjunction with the effectiveness of the 2013 Equity Incentive Plan (the 2013 Plan) described below, the Company determined that no further stock options or other equity-based awards may be granted under the 2003 Plan.

On September 4, 2013, the Board and stockholders approved the adoption of the 2013 Equity Incentive Plan (the 2013 Plan), which provides for the issuance of stock options, restricted stock units, and other equity-based awards. The Company has reserved for issuance an aggregate of 1,500,000 shares of common stock under the 2013 Plan which is comprised of (i) the remaining 155,884 shares reserved for issuance under the 2003 Plan and (ii) an additional 1,344,116 shares. The 2013 Plan provides that the number of shares reserved and available for issuance under the plan will automatically increase each January 1, beginning in 2014, by the lesser of (i) 3,150,000 shares, or (ii) 4% of the outstanding number of shares of the Company's common stock on the immediately preceding December 31st. This number is subject to adjustment in the event of a stock split, stock dividend or other change in the Company's capitalization. The number of shares underlying equity awards available for future grant was 3,555,548 at December 31, 2018.

The Company has not granted unrestricted stock awards under the 2003 Plan or the 2013 Plan since its inception. Stock options carry an exercise price equal to the estimated fair value of the Company's common stock on the date of grant. Options generally expire 10 years following the date of grant. Stock options typically vest over 4 years, and restricted stock units typically vest over 3 years, but vesting provisions can vary based on the discretion of the Board. Shares of the Company's common stock underlying any awards that are forfeited, canceled, withheld upon exercise of an option, or settlement of an award to cover the exercise price or tax withholding, reacquired by the Company prior to vesting, satisfied without the issuance of shares of the Company's common stock, or otherwise terminated other than by exercise will be added back to the shares of common stock available for issuance under the 2013 Plan. Shares available for issuance under the 2013 Plan may be authorized but unissued shares of the Company's common stock or shares of the Company's common stock that have been reacquired by the Company.

Additionally, on September 4, 2013, the Board and stockholders approved the adoption of the 2013 Employee Stock Purchase Plan (the 2013 ESPP). Under the 2013 ESPP, 275,000 shares of the Company's common stock will be available for issuance to eligible employees. The per-share purchase price at the end of each offering period is equal to 85% of the closing price of one share of the Company’s common stock at the beginning or end of the offering period, whichever is lower, subject to Internal Revenue Service limits. The 2013 ESPP will terminate on September 4, 2023, the tenth anniversary of the initial adoption of the plan. The Board determined the initial offering period commenced on September 16, 2014 and the initial purchase occurred on the 6 month anniversary with subsequent 6 month purchase periods commencing on the day following the purchase from the prior period. The Company recorded $0.4 million, $0.3 million, and $0.3 million of stock-based compensation expense during the years ended December 31, 2018, 2017, and 2016, respectively related to the 2013 ESPP. The number of shares available for future issuance was

155,948 at December 31, 2018.

In December 2016, the Company entered into a consulting agreement with its former Chief Executive Officer. In accordance with the 2003 Plan and 2013 Plan, any vested shares remain exercisable and any outstanding and unvested options and restricted stock units will continue to vest in accordance with their terms so long as he continues to provides services as a non-employee consultant. During the years ended December 31, 2018, 2017 and 2016, the Company recognized $2.4 million, $4.9 million, and $0.5 million, respectively, of stock-based compensation expense related to the agreement.

The Company recognized stock-based compensation expense under the various Plans in the consolidated statements of operations and comprehensive loss as follows (in thousands):

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Acceleron Pharma Inc.
Notes to Consolidated Financial Statements (Continued)
Years Ended December 31, 2018, 2017 and 2016

	Year Ended December 31,		
	2018	2017	2016
Research and development	$12,669	$14,227	$8,171
General and administrative	11,900	14,021	10,386
	$24,569	$28,248	$18,557

The fair value of each option issued to employees was estimated on the date of grant using the Black-Scholes option pricing model with the following weighted-average assumptions:

	Year Ended December 31,		
	2018	2017	2016
Expected volatility	62.8%	65.7%	65.1%
Expected term (in years)	6.0	6.0	6.0
Risk-free interest rate	2.70%	2.13%	1.69%