Akebia Therapeutics, Inc.
Form 10-K
March 06, 2017

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2016

OR

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 FOR THE TRANSITION PERIOD FROM TO
Commission File Number 001-36352

AKEBIA THERAPEUTICS, INC.

(Exact name of Registrant as specified in its Charter)

Delaware (State or other jurisdiction of incorporation or organization)	20-8756903 (I.R.S. Employer Identification No.)
245 First Street, Suite 1100, Cambridge, MA (Address of principal executive offices)	02142 (Zip Code)

Registrant’s telephone number, including area code: (617) 871-2098

Securities registered pursuant to Section 12(b) of the Act: Common Stock, Par Value $0.00001 Per Share; Common stock traded on the NASDAQ Global Market

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

Indicate by check mark if the Registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. YES NO

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. YES NO

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

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

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 Registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

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

Large accelerated filer Accelerated filer

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

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant, based on the closing price of the shares of common stock on The NASDAQ Stock Market on June 30, 2016, was $264,950,830.

The number of shares of Registrant's Common Stock outstanding as of March 1, 2017 was 38,829,563.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the definitive proxy statement for our 2017 Annual Meeting of Stockholders scheduled to be held June 15, 2017 are incorporated by reference into Part III of this annual report on Form 10-K.

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NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements that are being made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, or PSLRA, with the intention of obtaining the benefits of the "safe harbor" provisions of the PSLRA. Forward-looking statements involve risks and uncertainties. All statements other than statements of historical facts contained in this Annual Report on Form 10-K are forward-looking statements. In some cases, you can identify forward-looking statements by words such as "anticipate," "believe," "contemplate," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "target," "will," "would," the negative of these words or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- the projected timing of (1) our PRO_2TECT and $INNO_2$VATE clinical programs, and (2) our Phase 2 hyporesponder study, (3) our Phase 3 TIW dosing study, (4) submission of marketing applications for vadadustat, and (5) filing an IND for AKB-5169;
- enrollment in the PRO_2TECT and $INNO_2$VATE clinical programs;
- our development program for vadadustat in Japan;
- our anticipated funding from our collaborations;
- our plans to seek another geographic collaboration for the development and commercialization of vadadustat;
- our development plans with respect to vadadustat and our other product candidates;
- the timing or likelihood of regulatory filings and approvals, including any required post-marketing testing or any labeling and other restrictions;
- our plans to commercialize vadadustat, if it is approved;
- the implementation of our business model and strategic plans for our business, product candidates and technology;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our competitive position;
- our intellectual property position;
- developments and projections relating to our competitors and our industry;
- our estimates regarding expenses (including those associated with the PRO_2TECT and $INNO_2$VATE clinical programs), future revenue, capital requirements and needs for additional financing; and
- other risks and uncertainties, including those listed under Part I, Item 1A. Risk Factors.

All forward-looking statements in this Annual Report on Form 10-K involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under Part I, Item 1A. Risk Factors and elsewhere in this Annual Report on Form 10-K. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason.

This Annual Report on Form 10-K also contains estimates, projections and other information concerning our industry, our business, and the markets for certain diseases, including data regarding the estimated size of those markets, and the incidence and prevalence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainty and may prove inaccurate. Unless otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources.

PART I

Item 1. Business

Overview

We are a biopharmaceutical company focused on developing and delivering novel therapeutics for patients based on hypoxia-inducible factor, or HIF, biology, and building our pipeline while leveraging our development and commercial expertise in renal disease. HIF is the primary regulator of the production of red blood cells, or RBCs, in the body, as well as other important metabolic functions. Pharmacologic modulation of the HIF pathway may have broad therapeutic applications. Our lead product candidate, vadadustat, is an oral therapy in Phase 3 development, which has the potential to set a new standard of care in the treatment of anemia associated with chronic kidney disease (CKD). Our management team has extensive experience in developing and commercializing drugs for the treatment of renal and metabolic disorders, as well as a deep understanding of HIF biology. This unique combination of HIF and renal expertise is enabling us to advance a pipeline of HIF-based therapies to address serious diseases.

HIF, a pathway involving hundreds of genes, is responsible for orchestrating the body's natural response to lower levels of oxygen, or hypoxia. In response to hypoxia, a coordinated adaptive response occurs resulting in both an increase in red blood cell production, a normal biological process known as erythropoiesis, and enhancement of the delivery of iron to the bone marrow to support erythropoiesis. The significance of the HIF pathway was recognized by the 2016 Albert Lasker Basic Medical Research Award, which honored the three physician-scientists who discovered the HIF pathway and elucidated this primary oxygen sensing mechanism that is essential for survival. HIF protein is constantly being produced under normal oxygen conditions, but is quickly degraded by prolyl hydroxylases, or PH. Under hypoxic conditions, HIF-PH's are inhibited, allowing HIF to stimulate erythropoiesis. These findings have opened up new possibilities for developing therapeutics, such as HIF-PHI, which have the potential to treat many diseases.

Our lead product candidate, vadadustat, a HIF-PH inhibitor in Phase 3 development for the treatment of anemia of CKD. Anemia is a serious medical condition in which blood is deficient in hemoglobin, which is critical for delivering oxygen to organs and tissue. Untreated anemia is associated with chronic fatigue, increased risk of progression of multiple diseases and death. Anemia is common in patients with CKD, cancer, heart failure, inflammatory diseases and other critical illnesses.

More than 30 million people in the United States have CKD, with estimates that over 1.8 million of these patients suffer from anemia. Anemia from CKD is currently treated by injectable recombinant erythropoiesis-stimulating agents, or rESAs, such as EPOGEN® and Aranesp®, as well as with iron supplementation or red blood cell transfusion. Based on the reported revenues of companies that market and sell rESAs, global sales of injectable rESAs were estimated to be between $6.5 and $7.0 billion in 2015. The vast majority of these sales were for the treatment of anemia associated with renal disease.

rESAs deliver supra-physiological levels of exogenous erythropoietin, or EPO, to stimulate production of RBCs. While injectable rESAs may be effective in raising hemoglobin levels, they carry significant potential side effects, and need to be injected under the skin (subcutaneously) or into a vein (intravenously). In particular, injectable rESAs may lead to thrombosis, stroke, myocardial infarction and death. These safety concerns, which became evident starting in 2006, have led to a significant reduction in the use of injectable rESAs. Today, anemia is either not treated or inadequately treated in the majority of non-dialysis dependent (NDD) CKD patients. We believe that novel treatment options that address these concerns are needed and would have significant market potential. Because it mimics the body's natural adaptive response to hypoxia, vadadustat's HIF-PH inhibition may raise hemoglobin levels without

causing supra-physiological levels of EPO.

Vadadustat has the potential to set a new standard of care for the treatment of anemia in CKD. Early clinical studies of vadadustat demonstrated that diurnal variation of EPO was maintained resulting in predictable increases in hemoglobin in normal human volunteers and similar results were seen in NDD-CKD. These data led us to the design of our Phase 3 clinical program. The vadadustat Phase 3 program in NDD-CKD patients with anemia, called PRO_2TECT, and in dialysis dependent (DD) CKD patients with anemia, called $INNO_2VATE$, is designed to enroll approximately 5,700 patients evaluating once daily oral dosing of vadadustat against an rESA active comparator, darbepoetin alfa. The enrollment numbers and the completion of the Phase 3 program will be driven by the rate of major adverse cardiovascular events, or MACE. In December 2015 the first patient was dosed in PRO_2TECT, and the first patient was dosed in $INNO_2VATE$ in August 2016. We plan to initiate a Phase 3 study in the second half of 2017 to evaluate three-times weekly dosing of vadadustat in approximately 300 DD-CKD patients receiving hemodialysis using the same active comparator, darbepoetin alfa. We currently anticipate submitting marketing applications for the treatment of anemia associated with CKD in the United States and Europe in 2019.

If vadadustat is approved by the United States Food and Drug Administration, or FDA, we plan to establish our own commercial organization in the United States while leveraging our collaboration with Otsuka Pharmaceutical Co. Ltd., or Otsuka, and its well-established commercial organization. In Japan and other countries in Asia, we plan to commercialize vadadustat through our

collaboration with Mitsubishi Tanabe Pharma Corporation, or MTPC, and intend to seek one or more collaborators to commercialize vadadustat in Europe and other markets.

In addition to vadadustat, we are developing a HIF-based portfolio of product candidates that target serious diseases of high unmet need. Our portfolio includes product candidates developed internally, such as AKB-6899, as well as in-licensed product candidates, such as AKB-5169. AKB-6899 has demonstrated a robust hemoglobin response in early preclinical studies, and we plan to further investigate its potential in multiple preclinical models of anemia and assess next steps based on these data. In February 2017, we signed an agreement with Janssen Pharmaceutica NV, or Janssen, for access to an extensive library of well-characterized HIF pathway compounds with potential applications across multiple therapeutic areas. The lead compound, AKB-5169, is a differentiated preclinical compound in development as an oral treatment for inflammatory bowel disease (IBD) and we intend to complete further preclinical development with the goal of an Investigational New Drug application with the FDA in 2018.

Our Product Pipeline

Anemia Overview

Anemia is a term used to describe a decrease in RBCs. RBCs contain a protein called hemoglobin that is responsible for moving oxygen throughout the body. As a result, anemia is measured by the level of hemoglobin in the blood. Patients with CKD often have anemia because the kidneys do not make enough EPO, which stimulates the body to make RBCs. Less EPO causes the body to make fewer RBCs and hemoglobin, decreasing the supply of oxygen throughout the body. Anemia is a serious medical condition that exists when hemoglobin drops below 13 g/dL in men and 12 g/dL in women and, if left untreated, is associated with chronic fatigue, increased risk of progression of multiple diseases and death. Successful treatment of anemia significantly improves patients' quality of life and is associated with decreased cardiovascular morbidity, less frequent hospitalizations and lower mortality risk.

Chronic Kidney Disease

CKD, a common cause of anemia, is a condition in which the kidneys are progressively damaged to the point that they cannot properly filter the blood circulating in the body. This damage causes waste products to build up in the patient's blood leading to other health problems, including anemia, cardiovascular disease and bone disease. CKD patients are classified by the degree of their loss of kidney function as measured by the glomerular filtration rate, or GFR, and the level of protein in the urine, referred to as albuminuria. As illustrated in the table below, CKD affects more than 30 million people in the United States, and the prevalence of anemia increases with the severity of CKD.

There are many causes of CKD, including diabetes mellitus and hypertension. The prevalence and incidence of CKD is increasing in all segments of the United States population, particularly in patients over 65. Risk factors for the development of CKD include concomitant diseases (hypertension, diabetes mellitus and cardiovascular disease), lifestyle factors (tobacco use and inactivity), family history, aging and prenatal factors (maternal diabetes mellitus, low birth weight and small-for-gestational-age status). According to a Lancet article published in May 2013, projected worldwide population changes suggest that the potential number of cases of CKD, specifically end-stage, will increase disproportionately in countries, such as Japan, China and India, where the numbers of elderly people are increasing. This effect will be enhanced further if the growth in the prevalence of hypertension and diabetes persists along with the associated increased risk of stroke and cardiovascular disease and access to treatment does not improve.

Current Treatments Leave a Substantial Unmet Need

Injectable rESAs are currently the standard of care for treating anemia in patients with CKD and must be administered intravenously or subcutaneously along with iron supplements. In 2006, data on the risks of rESA use among these patients became available, forcing physicians to balance serious safety concerns against the efficacy of rESAs. The well-documented safety concerns[1] associated with the

[1] Besarab A, Bolton WK, Browne JK, Egrie JC, Nissenson AR, Okamoto DM, et al. The effects of normal as compared with low hematocrit values in patients with cardiac disease who are receiving hemodialysis and epoetin. N Engl J Med 1998;339(9):584-590.

Pfeffer MA, Burdmann EA, Chen CY, Coopper ME, de Zeeuw D, et al. A trial of darbepoetin alfa in type 2 diabetes and chronic kidney disease. N Engl J Med 2009;361(21):2019-2032.

Singh AK, Szczech L, Tang KL, Barnhart H, Sapp S, et al. Correction of anemia with epoetin alfa in chronic kidney disease. N Engl J Med 2006;355(20):2085-2098.

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use of injectable rESAs include increased cardiovascular risk, and the potential for increased rate of tumor progression in patients with cancer.

As a result of the safety concerns related to rESA use, patients live with lower hemoglobin levels, higher rates of RBC transfusions, and receive more intravenous iron, or IV iron, to treat anemia associated with CKD. The increased use of IV iron and RBC transfusions, also subject patients to safety risks related to these alternative treatments to injectable rESAs. The risks of RBC transfusions include the development of antibodies to foreign antigens, which may negatively impact candidacy for kidney transplantation, the potential transmission of blood-borne pathogens and iron overload with chronic transfusions. The risks of IV iron use include hypersensitivity reactions, including fatal anaphylactic-type reactions.

The graph below, based on a post hoc analysis of the Correction of Hemoglobin and Outcomes in Renal Insufficiency, or CHOIR, study suggests that patients achieving higher hemoglobin levels with lower injectable rESA doses had better outcomes than patients receiving higher injectable rESA doses despite lower achieved hemoglobin levels. Therefore, higher injectable rESA doses, not the achieved hemoglobin level, appeared to be most strongly correlated with adverse outcomes.

Vadadustat Has the Potential to Set a New Standard of Care

We believe that, based on the HIF-PH inhibition mechanism of action and clinical data to date, vadadustat has the potential to set a new standard of care for the treatment of anemia secondary to CKD. Below is a summary of the clinical findings and further details are included under the “Vadadustat Clinical Development Overview” section below.

- Vadadustat maintained a normal diurnal variation of EPO. In studies in healthy volunteers and CKD patients, vadadustat acted by simulating the body’s natural response to hypoxia and maintained a normal diurnal variation in EPO without causing supra-physiological levels of EPO.
- Vadadustat significantly increased and maintained hemoglobin levels. Our Phase 2 studies in CKD patients with anemia demonstrated that vadadustat significantly increased and/or maintained hemoglobin levels.

- Vadadustat has been studied as a once-daily or three times weekly oral dose. Phase 2 studies have shown that vadadustat can be orally dosed once daily in NDD-CKD patients over 20 weeks of dosing. In addition, a Phase 2 clinical study in DD-CKD patients demonstrated once daily or three times weekly oral dosing of vadadustat maintained stable hemoglobin levels in patients converting from ESA therapy over 16 weeks.
- Vadadustat improved mobilization of iron supply to the bone marrow for RBC production. In Phase 2 clinical studies, vadadustat demonstrated favorable changes in iron parameters (e.g. decrease in hepcidin and ferritin and increase in total iron binding capacity and transferrin saturation) consistent with improved iron mobilization to the bone marrow to support erythropoiesis in NDD-CKD and DD-CKD patients.

For the above reasons, we believe that vadadustat has the potential to demonstrate a reduced risk of cardiovascular (CV) and thrombotic events compared to injectable rESAs. These CV risks have been associated with supra-physiologic increases in EPO levels and excessive hemoglobin fluctuations and/or excursions beyond the target range. The incidence of CV adverse events associated with vadadustat as compared with darbepoetin alfa, an injectable rESA, is being assessed in the global Phase 3 program.

HIF-PH Inhibition: A Different Mechanism of Action That Mimics the Body's Natural Physiologic Response to Hypoxia

Vadadustat is designed to work by a mechanism of action that differs from injectable rESAs. This mechanism of action is referred to as HIF-PH inhibition. HIF is the primary regulator of the production of RBCs and acts by simulating the body's natural response to lower levels of oxygen, or hypoxia. In response to hypoxia, a coordinated adaptive response occurs resulting in both an increase in RBC production and enhancement of the delivery of iron to the bone marrow, ensuring the incorporation of iron into hemoglobin necessary for new RBC production. This is very similar to the body's natural adaptive response that is induced when a person ascends in altitude. At higher altitudes, lower levels of oxygen circulating in the blood stream lead to reduction in HIF-PH activity, which increases intracellular levels of HIFa proteins.

When stabilized, HIFa travels to the nucleus of the cell, where it binds to the protein HIFß. When bound together, they induce the production of EPO and iron transfer proteins. With continued stabilization of HIFa (either by staying at higher altitude or by the administration of a HIF-PH inhibitor), the level of hemoglobin and RBCs will rise in order to increase the amount of oxygen circulating in the blood.

Vadadustat Clinical Development Overview

In the 15 studies of vadadustat completed to date, the safety, tolerability, pharmacokinetic and pharmacodynamic properties of vadadustat have been demonstrated:

- nine completed Phase 1 studies in healthy volunteers (CI 0001, CI 0002, CI 0006, CI 0008, CI 0010, CI 0012, CI 0013, CI-0019, and CI-0020);
- one completed Phase 1 study in DD-CKD patients with anemia (CI 0009);
- three completed Phase 2a studies in NDD-CKD patients with anemia (CI 0003, CI 0004, and CI 0005);
- one completed Phase 2b study in NDD-CKD patients with anemia (CI 0007); and
- one completed Phase 2 study in DD-CKD patients with anemia (CI 0011).

The results from three of these key early studies are summarized below.

Vadadustat Clinical Development Summary

Vadadustat has been shown to maintain the normal diurnal variation in EPO levels without causing supra-physiological levels of EPO, while achieving the desired outcomes of raising and maintaining hemoglobin, and increasing iron mobilization to support erythropoiesis. Vadadustats safety profile has been consistent across Phase 1 and 2 studies completed to date. AEs identified as causally associated with vadadustat include mild to moderate nausea and diarrhea, as well as laboratory increases in uric acid levels not resulting in any further AEs.

Phase 1 Study in Normal Healthy Male Volunteers (CI-0002)

We have completed a Phase 1 randomized, double-blind, placebo-controlled, multiple-ascending dose study to evaluate the safety, tolerability, pharmacodynamics response, and pharmacokinetics of vadadustat administered for 10 days to healthy male volunteers. Dose responsive increases in reticulocytes, or immature RBCs, and hemoglobin levels were demonstrated in the study. EPO levels increased by 36%, 48%, 48%, and 110% over baseline in the placebo, 500 mg/day, 700 mg/day, and 900 mg/day at 16 hours after dosing and returned to baseline by 24 hours following each dose. The frequency of adverse events (AEs) was balanced between the combined vadadustat dosing groups (76%) and the placebo group (78%), and across vadadustat dosing cohorts. Gastrointestinal AEs occurred in 36% of subjects in the vadadustat groups and in no subjects on placebo, of which mild to moderate diarrhea was the most frequent (24%), but without a discernible dose related effect observed. No serious adverse events (SAEs) were reported in this study.

Phase 2b Study in Non-Dialysis CKD Patients (CI-0007)

We completed a multi-center Phase 2b study of vadadustat in subjects with anemia secondary to NDD-CKD. This double-blind, randomized, placebo-controlled study evaluated the efficacy and safety of vadadustat over 20 weeks of dosing in 210 subjects (138 vadadustat and 72 placebo) with CKD categories G3-G5. Subjects were enrolled into one of three groups: (1) ESA naïve with hemoglobin ≤10.5 g/dL, (2) previously treated with ESA with hemoglobin ≤10.5 g/dL, or (3) actively treated with ESA with hemoglobin ≥9.5 and ≤12.0 g/dL, and were randomized (2:1) to once daily vadadustat or placebo. The primary endpoint was the percent of subjects with either a mean hemoglobin of ≥11.0 g/dL or an increase in hemoglobin by ≥1.2 g/dL from baseline. A protocol-defined dose adjustment algorithm was used to achieve the primary endpoint and to minimize hemoglobin excursions ≥13 g/dL.

The average age was 66 years, ~75% of subjects had diabetes mellitus and the mean estimated glomerular filtration rate, or eGFR, was 25 mL/min/1.73m^2. 54.9% of vadadustat treated subjects compared to 10.3% of placebo treated subjects met the primary endpoint (p=0.0001). Only 4.3% of subjects in the vadadustat group had any hemoglobin excursion ≥13.0 g/dL. Group 3 placebo treated subjects experienced a decline in the mean hemoglobin within the first 2 weeks, whereas subjects randomized to vadadustat maintained a stable hemoglobin throughout the study. Increases in hemoglobin in the vadadustat group were associated with an increase in reticulocytes and total iron binding capacity, TIBC, and a decrease in serum hepcidin and ferritin. There was no difference between the vadadustat and placebo groups in vascular endothelial growth factor, or VEGF, levels during the study.

A similar percentage of subjects experienced AEs in the vadadustat and placebo treatment groups (74.6% vs. 73.6%). There was an increase in renal related SAEs reported in the vadadustat-treated subjects (vadadustat 9.4% vs. placebo 2.8%); however, the number of subjects requiring dialysis, an objective measure of the severity of renal disease, was similar in the two treatment groups (vadadustat 8.0% vs. placebo 9.7%). Overall AEs for renal and urinary disorders was balanced (vadadustat 14.5% vs. placebo 13.9%). The disparity in renal SAEs was likely related to variability in reporting between investigators (reasons included proceeding to dialysis in association with a SAE that was not reported in the renal category, or proceeding to dialysis without being considered an SAE). Other differences in AEs, favoring either vadadustat or placebo, were as follows: nausea and diarrhea (vadadustat 10.1% vs. placebo 4.2%); gastrointestinal hemorrhage (vadadustat 0.0% vs. placebo 5.6%); upper respiratory tract infection (vadadustat 1.4% vs. placebo 6.9%); hyperkalemia (vadadustat 5.1% vs. placebo 0.0%); and hypertension (vadadustat 8.0% vs. placebo 2.8%). There were three deaths in vadadustat-treated subjects (two were considered to be unrelated to vadadustat and one was considered by the investigator to be possibly related because no autopsy was performed to rule out relatedness) and there were no deaths in the placebo group.

In summary, vadadustat achieved the desired outcomes of raising and maintaining hemoglobin and increasing iron mobilization, while minimizing hemoglobin excursions ≥13 g/dL. Pergola et al published the results of this study in Kidney International 2016.

Phase 2 Study in Dialysis-Dependent CKD Patients (CI-0011)

We have completed a multi-center, open-label, 16-week study to assess the hemoglobin response, safety, and tolerability of vadadustat in DD-CKD subjects. The study enrolled 94 hemodialysis subjects (hemoglobin 9-12 g/dL), who were maintained on ESAs prior to study entry. Subjects were converted from ESA to vadadustat, and assigned to 1 of 3 dose cohorts: 300 mg once daily (QD); 450 mg QD; or 450 mg three times weekly (TIW). For each dose cohort, the mean or average hemoglobin level at study entry was compared to the average hemoglobin level at weeks 7 and 8, and to the average hemoglobin level at weeks 15 and 16. To evaluate hemoglobin response to each of the dose regimens, during the first eight weeks of this study subjects were to remain on the prescribed starting dose, or decreased if necessary to control hemoglobin in the target range. Beginning at week eight, the dose of vadadustat could be increased or decreased to maintain hemoglobin levels as needed. Intravenous iron use was allowed.

The underlying patient demographics and profile of these CKD patients were well-balanced across the three cohorts, and reflective of the United States DD-CKD population as reported in the literature. Average age was 58 years, with an average time on dialysis of 4.6 years. The most common cause of end-stage renal disease was diabetes mellitus and/or hypertension. Baseline hemoglobin levels were

similar (10.4-10.6 g/dL) in all three cohorts and the serum ferritin levels indicated that the subjects were iron replete at study entry and throughout the study.

The study achieved its primary endpoint of maintaining stable hemoglobin levels over 16 weeks, across all three cohorts of subjects converting from ESAs to vadadustat. The study supports both daily and three times weekly vadadustat dosing regimens as viable options. Consistent with previous studies, all three starting dose regimens suggested an improvement in iron mobilization, as reflected by increases in total iron binding capacity and serum iron, and decreases in serum ferritin and hepcidin levels. Only one subject in the 300 mg once daily cohort had a single hemoglobin excursion to 13.1 g/dL.

Mean Hemoglobin Levels (g/dL)*	Baseline	Week 7/8	Week 15/16
300mg Daily Dose	10.4	10.4	10.3
450mg Daily Dose	10.6	10.3	10.5
450mg Three Times per Week Dose	10.5	10.2	10.4

*Modified intent-to-treat (MITT) population, n=94

Adverse events were balanced across the three cohorts. There were no discernible trends in the frequency of AEs or SAEs by dose cohort. SAEs were reported in 13 subjects (13.8%); no SAEs were reported as related to vadadustat and no deaths occurred during the study.

The results of this study demonstrate that vadadustat maintained hemoglobin levels in DD-CKD subjects who were converted from existing ESA therapy to vadadustat. Only one subject had a single hemoglobin excursion to a level of 13.1 g/dL. The frequency and type of SAEs were consistent with those expected in a DD-CKD population. The results of this study were reported at the American Society of Nephrology meeting in November 2015 and the National Kidney Foundation Spring Clinical Meeting in April 2016.

Phase 3 Global Program

We are conducting two global Phase 3 studies to support an indication for the treatment of anemia in NDD-CKD patients and three global Phase 3 studies to support an indication for the treatment of anemia in DD-CKD patients:

1. CI-0014: “Phase 3, Randomized, Open-Label, Active-Controlled Study Evaluating the Efficacy and Safety of Oral Vadadustat for the Correction of Anemia in Subjects with Non-Dialysis-Dependent Chronic Kidney Disease (NDD CKD) (PRO2TECT - CORRECTION)”
2. CI-0015: “Phase 3, Randomized, Open-Label, Active-Controlled Study Evaluating the Efficacy and Safety of Oral Vadadustat for the Maintenance Treatment of Anemia in Subjects with Non-Dialysis-Dependent Chronic Kidney Disease (NDD CKD) (PRO2TECT CONVERSION)”
3. CI-0016: “Phase 3, Randomized, Open-Label, Active-Controlled Study Evaluating the Efficacy and Safety of Oral Vadadustat for the Correction of Anemia in Subjects with Dialysis-Dependent Chronic Kidney Disease (DD CKD) (INNO2VATE - CORRECTION)”
4. CI-0017: “Phase 3, Randomized, Open-Label, Active-Controlled Study Evaluating the Efficacy and Safety of Oral Vadadustat for the Maintenance Treatment of Anemia in Subjects with Dialysis-Dependent Chronic Kidney Disease (DD-CKD) (INNO2VATE CONVERSION)”
5. CI-0023: “Phase 3, Randomized, Open-Label, Active-Controlled Study Evaluating the Efficacy and Safety of Oral Vadadustat Dosed Three Times Weekly for the Maintenance Treatment of Anemia in Subjects with

Dialysis-Dependent Chronic Kidney Disease (DD-CKD) (TIW Phase 3 Study)"

In both the PRO_2TECT and $INNO_2$VATE Phase 3 programs, the primary efficacy endpoint is the mean change in hemoglobin between baseline (mean pretreatment hemoglobin) and the primary evaluation period, concluding non-inferiority (NI) when the upper 95% confidence interval of the hazard ratio (vadadustat/darbepoetin alfa) does not exceed the NI margin. Both the PRO_2TECT and $INNO_2$VATE programs will include the primary safety endpoint of the assessment of major adverse cardiovascular endpoints, or MACE, with a comparison of vadadustat to darbepoetin alfa. MACE is defined as the composite endpoint of all-cause mortality, non-fatal myocardial infarction, or non-fatal stroke. To assess MACE, a pooled analysis of time to first MACE event from the two Phase 3 studies in each program will be performed, concluding NI when the upper 95% confidence interval of the hazard ratio (vadadustat/darbepoetin alfa) does not exceed the NI margin. We obtained feedback from the United States and European regulatory authorities regarding the design of these programs.

Overall, the PRO$_2$TECT and INNO$_2$VATE Phase 3 programs are designed to enroll approximately 5,700 CKD patients. We have engaged Quintiles IMS as our primary clinical contract research organization, or CRO, for the PRO$_2$TECT and INNO$_2$VATE programs. We expect the cost of the PRO$_2$TECT and INNO$_2$VATE programs to be in the range of $80,000 to $85,000 per patient, aggregating in the range of $456.0 million to $484.5 million in external CRO costs for the total program. Such estimated costs could increase significantly if the Phase 3 program takes longer to complete or if we choose to add additional investigative sites, add additional patients, modify the clinical trial protocol, or perform other studies in support of the Phase 3 program.

Based on a Phase 2 study (CI-0011), which demonstrated that vadadustat administered once-daily or three-times weekly maintained hemoglobin levels in hemodialysis subjects who were converted from existing ESA therapy, we plan to initiate a Phase 3 study of three-times weekly dosing. This study will enroll approximately 300 DD-CKD patients receiving hemodialysis and will begin in the second half of 2017, and expect to have topline clinical data in 2018. Patients receiving maintenance hemodialysis typically receive their treatments three-times weekly and the flexibility of administering vadadustat three-times weekly on the day of their dialysis session would be desirable. Furthermore, we have shown that the hemodialysis procedure does not have a significant impact on the pharmacokinetics of vadadustat or its metabolites, indicating that vadadustat can be administered irrespective of the timing of the dialysis session (CI-0009).

Additional Studies

We have completed a thorough QT, or TQT, study in accordance with FDA guidance and confirmed that vadadustat does not alter cardiac repolarization intervals in healthy volunteers following a single dose of up to 1200 mg. In addition, we completed a drug-drug interaction study that demonstrated there is no impact of vadadustat on the metabolism of any of the major statins, which are commonly prescribed for CKD patients.

We plan to initiate a Phase 2 study in DD-CKD patients who do not have an adequate hemoglobin response despite receiving high doses of rESAs. This represents approximately 10-15% of DD-CKD patients. Previous studies have shown that rESA hyporesponsiveness is associated with poor clinical outcomes, including increased mortality risk. By increasing iron mobilization, in addition to erythropoietin levels, vadadustat may allow for a more consistent hemoglobin response in these patients. We plan to initiate the rESA hyporesponder study in the second half of 2017, and expect to have clinical data in 2018.

Manufacturing and Supply

Vadadustat is a small molecule that is manufactured from readily available commercial starting materials. We have no internal manufacturing capabilities and rely on third-party contract manufacturers to produce all lots of drug substance and drug products.

We have a Master Services Agreement with Evonik Corporation, or Evonik, pursuant to which Evonik develops and manufactures vadadustat drug substance for use in our Phase 3 development program and in other clinical trials. Evonik is currently manufacturing vadadustat at commercially-relevant scale. We also have a Master Services Agreement with Esteve Quimica, or Esteve, to manufacture vadadustat for clinical trial use.

The drug substance can be readily formulated into compressed tablets with pharmacopeial excipients using common manufacturing processes. We have a Master Services Agreement with UPM, pursuant to which UPM further develops and manufactures the drug product for use in our Phase 3 global program for vadadustat and other clinical trials. UPM is currently manufacturing vadadustat tablets at commercially relevant scale.

In our agreements with third-party manufacturers, we retain ownership of our intellectual property and generally own and/or are licensed rights to processes, developments, data, results and other intellectual property relating to our products and generated during the course of the manufacturer's performance under the agreement. We retain the right to source drug substance and drug product from multiple suppliers.

Strategic Collaborations

Collaboration with Otsuka Pharmaceutical Co. Ltd.

On December 18, 2016, we entered into a Collaboration and License Agreement with Otsuka, pursuant to which we agreed to co-exclusively collaborate with Otsuka with respect to the development and commercialization of vadadustat in the United States. Under the Agreement, the parties will co-exclusively commercialize vadadustat in the United States, subject to approval of vadadustat by the FDA. We will continue to lead the ongoing global Phase 3 development program for vadadustat.

Under the terms of the agreement, Otsuka paid us an upfront payment of $125.0 million and are committed to provide additional funding of $140.0 million or more toward the vadadustat global development program. In addition, if the development costs exceed a certain threshold, we may require Otsuka to pay a higher percentage of the global development costs. In such event, Otsuka would be

reimbursed for such additional funding out of milestone payments and net sales of vadadustat in the United States. In addition, we are eligible to receive from Otsuka up to $765.0 million in specified development and commercial milestones.

The agreement establishes a profit share for the commercialization of vadadustat in the United States. Under the agreement, the parties will equally share all net sales of vadadustat in the United States, and each party will bear half of all costs in the United States (including medical affairs, commercialization and manufacturing costs).

Collaboration with Mitsubishi Tanabe Pharma Corporation

On December 11, 2015, we and MTPC entered into a collaboration agreement providing MTPC with exclusive development and commercialization rights to vadadustat in Japan and certain other Asian countries.

In consideration for the exclusive license and other rights contained in the agreement, MTPC will make payments totaling up to $100.0 million to fund the vadadustat global Phase 3 program, including $40.0 million paid in 2016. To the extent Japanese patients are included in the Phase 3 Program, MTPC will fund up to an additional $60.0 million of development costs. If Japanese patients are not included in the Phase 3 Program, MTPC will be responsible for the costs of the local Phase 3 study in Japan and will make no additional funding payments for the Phase 3 Program, and $20.0 million of the $40.0 million we received in 2016 would be used to fund local development of vadadustat in Japan or be refunded to MTPC, at MTPC's discretion. In addition, we are eligible to receive up to approximately $250.0 million in additional milestone payments, based upon achievement of certain development and sales milestones. MTPC also agreed to make tiered royalty payments, from low teens up to twenty percent, on sales of vadadustat in the territory.

Intellectual Property

The proprietary nature of, and protection for, our product candidates and our discovery programs, processes and know-how are important to our business. Our policy is to seek to protect our proprietary position by, among other methods, filing United States 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 know-how, continuing technological innovation and potential in-licensing opportunities to develop and maintain our proprietary position. Additionally, we may benefit from a variety of statutory frameworks in the United States, Europe and other countries that provide periods of non-patent-based exclusivity for qualifying molecules. See "—Regulatory Matters."

Our commercial success will depend in part on obtaining and maintaining patent protection of our current and future product candidates, methods of their use and the methods used to develop and manufacture them, as well as successfully defending these patents against third-party challenges. Our ability to stop third parties from making, using, selling, offering to sell or importing our products depends on the extent to which we have rights under valid and enforceable patents that cover these activities. We cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be commercially useful in protecting our product candidates, discovery programs and processes. Even once patents successfully issue, third parties may challenge the validity, enforceability, inventorship, or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. For this and more comprehensive risks related to our intellectual property, please see "Risk Factors—Risks Related to Our Intellectual Property."

Our patent estate, on a worldwide basis, includes 109 allowed applications and issued patents and approximately 125 pending utility and provisional patent applications, with pending and issued claims relating to our current clinical stage candidate vadadustat as well as other product candidates, including AKB-6899. We also hold three patents that

claim the crystal of a protein-ligand complex comprising a protein-ligand complex of hypoxia inducible factor-1 alpha prolyl hydroxylase as well as methods for identifying compounds that bind to hypoxia inducible factor-1 alpha prolyl hydroxylase.

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 20 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 20 years from the earliest international filing date. Patent term recapture for loss of term as a result of the regulatory review period is available in some foreign jurisdictions. Our issued patents and pending applications with respect to our composition of matter, methods of treatment, and pharmaceutical compositions are expected to expire in 2027 or 2028 (depending on eligibility for patent term adjustment) and our pending applications with respect to processes for manufacturing vadadustat, dosing regimens,

formulations, and various other aspects relating to the treatment of anemia using vadadustat are expected to expire between 2032 and 2034, exclusive of possible patent term adjustments or 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.

Changes in either the patent laws or 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.

Vadadustat Patent Portfolio

We hold five issued patents and one allowed application covering the composition of matter, method of treating anemia, and pharmaceutical compositions of vadadustat in the United States, one issued patent in Europe (registered in most countries of the European Patent Convention), and additional patents issued or pending in many other major jurisdictions worldwide, including Japan, China, South Korea, Brazil, Mexico, Russia, Israel and India. The expected expiration date for these composition of matter patents is 2028 plus any extensions or adjustments of term available under national law.

In July of 2011, a third party filed an opposition to our issued European Patent No. 2044005 (the ’005 Patent). During the oral proceedings, which took place on April 10, 2013, the Opposition Division of the European Patent Office maintained the ’005 Patent on the basis of the third auxiliary request filed during the oral proceedings. This decision resulted in the maintenance of a claim directed to a compound chosen from a group of eight compounds, including vadadustat, as well as claims to compositions and methods for treating various diseases, including, but not limited to, anemia. Both parties have appealed the decision of the Opposition Division and final resolution of the opposition proceedings will likely take a number of years. We cannot be assured of the breadth of the claims that will remain in the ’005 Patent or that the patent will not be revoked in its entirety.

We also hold patents and patent applications directed to processes for manufacturing vadadustat, dosing regimens, formulations, polymorphs, and various other aspects relating to the treatment of anemia using vadadustat that are expected to expire between 2032 and 2034 exclusive of possible patent term extensions.

AKB-6899 Patent Portfolio

We hold four issued patents covering the AKB-6899 composition of matter, pharmaceutical compositions, and methods of treating anemia by administration of AKB-6899, respectively, in the United States, and additional patents issued or pending in many other major jurisdictions worldwide, including Europe, Japan, China, South Korea, Brazil,

Mexico, Russia and India. The expected expiration date for these composition of matter patents is 2028 plus any extensions or adjustments of term available under national law.

We also hold, either alone or jointly, one issued patent and one pending application covering various methods, including, but not limited to, the treatment of cancer by administration of AKB-6899 in the United States and additional patent applications are issued or pending in many other major jurisdictions worldwide, including Japan, China, South Korea, Mexico, Russia, Israel and India. The expected expiration dates for these method of treatment patent applications are expected to be 2032 exclusive of possible patent term extensions or adjustments. We hold one pending patent application in the United States and approximately 13 pending patent applications worldwide directed to treatment or prevention of ocular conditions using AKB-6899, and one pending patent application in the United States and approximately 30 pending patent applications worldwide directed to dosing regimens of AKB-6899. The expected expiration date of this ocular patent application is 2035, and the expected expiration date of this dosing patent application is 2034, exclusive of possible patent term extensions or adjustments. We hold four pending patent applications in various foreign

jurisdictions and a pending international application directed to polymorphs of AKB-6899. The expected expiration date of this polymorph patent application is 2036 exclusive of possible patent term extensions or adjustments.

AKB-5169 Patent Portfolio

There are three issued patents and one pending patent application covering the AKB-5169 composition of matter, pharmaceutical compositions, and methods of treating anemia by administration of AKB-5169, respectively, in the United States, and additional patents issued or pending in many other major jurisdictions worldwide, including Europe, Japan, China, Brazil, Russia and India. The expected expiration date for these composition of matter patents is 2029 plus any extensions or adjustments of term available under national law.

Know-How

In addition to patents, we rely upon unpatented know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary information, in part, using confidentiality agreements with our collaborators, employees and consultants and invention assignment provisions in the confidentiality agreements with our employees. These agreements are designed to protect our proprietary information and, in the case of the invention assignment provisions, to grant us ownership of technologies that are developed by our employees. These agreements may be breached, and we may not have adequate remedies for any breach.

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.

Third-Party Filings

We are aware of certain United States patents issued to FibroGen, Inc., or FibroGen, directed to, among other things, purportedly new methods of using previously known heterocyclic carboxamide compounds for purposes of treating or affecting specified conditions. We do not believe these currently issued FibroGen United States patents conflict with our intellectual property rights; nor do we make any admission that any of such patents are valid or enforceable. Under United States law, a person may be able to patent a discovery of a new way to use a previously known compound, even if such compound itself is patented, provided, the newly discovered use is novel and non-obvious. Such a method-of-use patent, however, if valid, only protects the use of a claimed compound for the specified methods claimed in the patent. This type of patent does not prevent persons from using the compound for any previously known use of the compound. Further, this type of patent does not prevent persons from making and marketing the compound for an indication that is outside the scope of the patented method. We are not aware of any valid United States patents issued to FibroGen that claim methods of using any of our product candidates for purposes of inhibiting HIF-PHs for the treatment of anemia secondary to CKD.

We have had a number of positive developments in our opposition and invalidity proceedings against FibroGen. With regard to the opposition that we filed in Europe against FibroGen's European Patent No. 1463823, or the '823 patent, an oral proceeding took place March 8 and 9, 2016. Following the oral proceeding, the European Opposition Division ruled that the patent as granted did not meet the requirements for patentability under the European Patent Convention and, therefore, revoked the patent in its entirety. FibroGen has appealed that decision. Likewise, with regard to the invalidity proceeding that we filed in Japan against certain claims of FibroGen's Japanese Patent No. 4804131, or the '131 patent, which is the Japanese counterpart to the '823 patent, the Japan Patent Office, or JPO, issued a preliminary decision finding all of the challenged claims to be invalid. FibroGen subsequently amended the claims and the JPO accepted the amendments. The resulting FibroGen Japanese '131 patent does not cover vadadustat or any pyridine carboxamide compounds. To date, FibroGen has been unsuccessful in its attempts to obtain a patent in the United States covering the same claim scope as it obtained initially in Europe and Japan in the '823 and '131 patents. In the

event FibroGen were to obtain such a patent in the United States, we may decide to challenge the patent like we have done in Europe and Japan.

On May 13, 2015, May 20, 2015 and July 6, 2015 we filed oppositions to FibroGen's European Patent Nos. 2322153, 2322155, and 163333, or the '153 patent, the '155 patent, and the '333 patent, respectively, requesting the patents be revoked in their entirety. These related patents claim, among other things, various compounds that either stabilize HIF or inhibit a HIF hydroxylase or a HIF prolyl hydroxylase for treating or preventing various conditions, including, inter alia, iron deficiency, microcytosis associated with iron deficiency, anemia of chronic disease, anemia wherein the subject has a transferrin saturation of less than 20%, anemia refractory to treatment with exogenously administered erythropoietin, or EPO, and microcytosis in microcytic anemia. Such method of use patents do not prevent persons from using the compound for other uses, including any previously known use of the compound. In particular, these patents do not claim methods of using any of our product candidates for purposes of inhibiting hypoxia-inducible factor prolyl hydroxylases, or HIF-PHs, for the treatment of anemia secondary to CKD. While we do not believe these patents will prevent us from commercializing vadadustat for treatment of anemia secondary to CKD, we filed these oppositions to provide us and any future partners with maximum flexibility for developing vadadustat and our pipeline of HIF PH inhibitors. With regard to the opposition that

we filed in Europe against FibroGen's European Patent No. 163333, or the '333 patent, an oral proceeding took place December 8 and 9, 2016. Following the oral proceeding, the European Opposition Division ruled that the patent as granted did not meet the requirements for patentability under the European Patent Convention and, therefore, revoked the patent in its entirety. FibroGen has appealed that decision. Oppositions to the '155 patent and to the '153 patent were also filed by Glaxo Group Limited, or Glaxo, and by Bayer Intellectual Property GmbH, Bayer Pharma Aktiengesellschaft, and Bayer Animal Health GmbH. While, for the reasons set forth in our oppositions, we believe that the '153 patent and the '155 patent should be revoked in their entirety, the ultimate outcomes of the oppositions remains uncertain.

Competition

If vadadustat is approved and launched commercially, competing drugs may include EPOGEN® and Aranesp®, commercialized by Amgen, Procrit® and Eprex®, commercialized by Johnson & Johnson, and Mircera®, commercialized by Roche Holding Ltd., or Roche. In Europe and other markets biosimilar versions of rESAs are available and may become available in the United States in the future. We may face competition from potential new anemia therapies. There are several other HIF-PHI product candidates in various stages of active development for anemia indications that may be in direct competition with vadadustat if and when they are approved and launched commercially. These candidates are being developed by such companies as FibroGen, in collaboration with AstraZeneca PLC in the United States and China and with Astellas Pharma Inc. in Europe and Asia, Japan Tobacco International, GlaxoSmithKline plc and Bayer HealthCare AG. FibroGen is currently in Phase 3 clinical development of its product candidate, roxadustat, and GlaxoSmithKline plc recently commenced Phase 3 studies of its product candidate, daprodustat. Some of these product candidates may enter the market as early as 2017.

Regulatory Matters

The FDA, and comparable regulatory authorities in other countries impose substantial and burdensome requirements upon companies involved in the clinical development, manufacture, marketing, labeling and packaging, storage, distribution, post-approval monitoring and reporting, advertising and promotion, pricing, and export and import of drugs. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. Moreover, failure to comply with applicable regulatory requirements may result in, among other things, warning or untitled letters, clinical holds, civil or criminal penalties, recall or seizure of products, injunction, disbarment, denial of marketing approval, partial or total suspension of production, and/or for approved products, withdrawal of the product from the market. Any agency or judicial enforcement action could have a material adverse effect on us.

U.S. Government Regulation

In the United States, the FDA regulates drug products under the Federal Food, Drug, and Cosmetic Act, or FD&C Act, all amendments thereto, and its implementing regulations. If we fail to comply with applicable FDA or other requirements at any time during the drug development process, clinical testing, approval process or after approval, we may become subject to administrative or judicial sanctions. These sanctions could include the FDA's refusal to approve pending applications, license suspension or revocation, clinical trial hold or suspension, withdrawal of an approval, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties or criminal prosecution. Any FDA enforcement or administrative action could have a material adverse effect on us.

FDA approval is required before any new unapproved drug or dosage form, including a new use of a previously approved drug, can be marketed in the United States. The process required by the FDA before a drug may be marketed in the United States generally involves:

- completion of extensive preclinical laboratory tests, preclinical animal studies and formulation studies performed in accordance with the FDA's current Good Laboratory Practice, or cGLP, regulations;
- submission to the FDA of an Investigation New Drug, or IND application, which must become effective before human clinical trials in the United States may begin;
- approval by an institutional review board, or IRB, or ethics committee, or EC, before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials to establish the safety and efficacy of the drug candidate for each proposed indication;
- submission to the FDA of a New Drug Application or NDA;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with current cGMP regulations;

- satisfactory completion of a potential review by an FDA advisory committee, if applicable; and
- FDA review and approval of the NDA prior to any commercial marketing, sale or commercial shipment of the drug in the United States.

The manufacturing, nonclinical testing, clinical testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for our product candidates will be granted on a timely basis, if at all. Nonclinical tests include laboratory evaluation of product chemistry, formulation, stability and toxicity, as well as animal studies to assess the characteristics and potential safety and efficacy of the product.

The results of nonclinical tests, together with manufacturing information, analytical data and a proposed clinical trial protocol, and other information, are submitted FDA as part of an IND. The central focus of an IND submission is on the general investigational plan and the protocol(s) for first-in human study (ies). Some nonclinical testing may continue even after the IND is submitted, but an IND must become effective before human clinical trials may begin in the United States. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises concerns or questions relating to one or more proposed clinical trials and places the clinical trial on a clinical hold, including concerns that human research subjects will be exposed to unreasonable health risks. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Accordingly, submission of an IND may or may not result in the FDA allowing clinical trials to commence. A separate amendment to an existing IND must also be made for each successive clinical trial conducted during product development.

Clinical trials involve the administration of the investigational drug to human subjects under the supervision of qualified investigators in accordance with Good Clinical Practices, or cGCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, the parameters to be used in monitoring safety and the effectiveness criteria to be used. Each protocol in the United States must be submitted to the FDA as part of the IND. In addition, an independent institutional review board, or IRB, or ethics committee for each medical center proposing to conduct a clinical trial must also review and approve a plan for any clinical trial before it can begin at that center and the IRB must monitor the clinical trial until it is completed. There are also requirements governing the reporting of ongoing clinical trials and clinical trial results to public registries.

A sponsor who wishes to conduct a clinical trial outside the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the sponsor may submit data from the clinical trial to the FDA in support of an NDA, if certain requirements are met. Per FDA regulations, the clinical trial must be conducted either: 1) in compliance with an international guideline for the ethical conduct of clinical research known as the Declaration of Helsinki or 2) with the laws and regulations of the country or countries in which the clinical trial is performed, whichever provides the greater protection to the participants in the clinical trial.

Government Regulation Outside U.S.

In addition to regulations in the United States, we will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries.

Certain countries outside of the United States have a similar process that requires the submission of a clinical trial application, or CTA, much like the IND, prior to the commencement of human clinical trials. In Europe, for example, a CTA must be approved by each country’s national health authority and an independent ethics committee, much like the FDA and IRB, respectively. Once the CTA is approved in accordance with a country’s requirements, the clinical

trial may proceed. Outside of the United States, each clinical trial to be conducted in a given country requires submission and approval of a unique CTA.

The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, the clinical trials are conducted in accordance with cGCP requirements and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. To obtain regulatory approval of an investigational drug under European Union, or EU, regulatory systems, we must submit a Marketing Authorization Application, or MAA. To obtain regulatory approval of an investigational drug under Japanese regulatory systems, we must submit a Japanese NDA. The application used to file the NDA in the United States is similar to that required in Europe and Japan, with the exception of, among other things, country-specific document requirements.

An approved Paediatric Investigation Plan (PIP) is required in Europe prior to submission of the MAA. Ideally, the pediatric studies in both the U.S. Pediatric Study Plan and the EU PIP will be identical, but some differences may be required to meet the respective

regulatory requirements (e.g., waiver age). The PIP outlines the study designs and timing of the pediatric program. The EMA Paediatric Committee and the FDA's Office of Pediatric Therapeutics have frequent joint discussions about pediatric drug development, including discussions about specific drugs. Often, these discussions are conducted in an attempt to harmonize pediatric drug development across the two jurisdictions. However, this cannot be guaranteed.

For other countries outside of the European Union, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, again, the clinical trials must be conducted in accordance with cGCP requirements and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Clinical Trials

Clinical trials are typically conducted in three or four phases, which may overlap or be combined:

- Phase 1: Clinical trials are initially conducted in a limited population of subjects to test the drug candidate for safety, dose tolerance, absorption, metabolism, distribution and excretion in healthy humans or, on occasion, in patients with severe problems or life threatening diseases to gain an early indication of its effectiveness.
- Phase 2: Clinical trials are generally conducted in a limited patient population to evaluate dosage tolerance and appropriate dosage, identify possible adverse effects and safety risks, and evaluate preliminarily the efficacy of the drug for specific targeted indications in patients with the disease or condition under study.
- Phase 3: Clinical trials are typically conducted when Phase 2 clinical trials demonstrate that a dose range of the product candidate is effective and has an acceptable safety profile. Phase 3 clinical trials are commonly referred to as "pivotal" studies, which typically denotes a study that the FDA or other relevant regulatory agencies will use to determine whether or not to approve a drug. Phase 3 clinical trials are generally undertaken with large numbers of patients, such as groups of several hundred to several thousand, to further evaluate dosage, to provide substantial evidence of clinical efficacy and to further test for safety in an expanded and diverse patient population at multiple, geographically-dispersed clinical trial sites.
- Phase 4: In some cases, FDA may condition approval of an NDA for a product candidate on the sponsor's agreement to conduct additional clinical trials after NDA approval. In other cases, a sponsor may voluntarily conduct additional clinical trials post-approval to gain more information about the drug. Such post approval trials are typically referred to as Phase 4 clinical trials.

The FDA, the IRB, or the sponsor may suspend or discontinue a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides recommendations for whether or not a trial may move forward at designated check points based on access to certain data from the study.

Concurrent with clinical trials, companies usually complete additional animal testing and must also develop additional information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing the drug in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality, purity and potency of the final drug product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its intended shelf life at the intended storage condition.

New Drug Applications

The clinical trials, together with the results of nonclinical studies and extensive manufacturing information and information on the composition of the drug, are submitted to the FDA in the form of an NDA requesting approval to market the drug for one or more specified indications. The FDA reviews an NDA to determine, among other things, whether a drug is safe and effective for its intended use.

Once the NDA submission has been accepted for review, under the Prescription Drug User Fee Act, or PDUFA, the FDA has a goal of responding to standard review NDAs within ten months after the 60-day filing review period, but this timeframe is often extended. The first indication of the FDA's review progress is provided at the mid-cycle review. This typically occurs five months after the NDA is accepted for review. However, the review process is often significantly extended by FDA requests for additional information or clarification. The FDA may refer the application to an advisory committee for review, evaluation and recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations.

Before approving an application, the FDA will inspect the facility or the facilities at which the finished drug product, and sometimes the active drug ingredient, is manufactured, and will not approve the drug unless cGMP compliance is satisfactory. The FDA may also inspect the sites at which the clinical trials were conducted to assess their compliance, and will not approve the drug unless compliance with GCP requirements is satisfactory.

After the FDA evaluates the NDA and conducts inspections of manufacturing facilities, it may issue an approval letter or a Complete Response Letter (CRL). An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A CRL indicates that the review cycle of the application is complete but the application is not yet ready for approval. A CRL may require additional clinical data and/or other significant, expensive, and time-consuming requirements related to clinical trials, nonclinical studies and/or manufacturing. Even if such data are submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Data from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret data. The FDA could also approve the NDA with a Risk Evaluation and Mitigation Strategy, or REMS, requirement to mitigate risks, which could include medication guides, physician communication plans, or elements to ensure safe use, such as restricted distribution programs, patient registries or other risk minimization tools. The FDA may also condition approval on, among other things, changes to proposed labeling, development of adequate controls and specifications, or a commitment to conduct one or more post-market studies or clinical trials. Such post-market testing may include Phase 4 clinical trials and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

An approved Pediatric Study Plan, or PSP, is required for vadadustat under the Pediatric Research Equity Act prior to submission of the NDA. The PSP outlines the study designs and timing of the pediatric program. Once the PSP is approved, Akebia and FDA will have reached agreement on the pediatric studies necessary for vadadustat, any deferrals from pediatric data to be included in the NDA, and any waivers of pediatric age ranges in which vadadustat need not be studied.

Once the FDA approves an NDA, or supplement thereto, the FDA may withdraw the approval if ongoing regulatory requirements are not met or if safety problems are identified after the drug reaches the market. Where a withdrawal may not be appropriate, the FDA still may seize existing inventory of such drug or request a recall of any drug already on the market. In addition, the FDA has the authority to prevent or limit further marketing of a drug based on the results of post-market studies or surveillance programs.

After regulatory approval of a drug is obtained, companies are subject to a number of post-approval requirements. For example, there are reporting obligations regarding certain adverse events received and production problems. Companies are also required to report updated safety and efficacy information, and to comply with requirements concerning advertising and promotional labeling. Drugs may be marketed only for the FDA-approved indications and in accordance with the provisions of the approved labeling. The FDA strictly regulates labeling, advertising, promotion and other types of information on products that are placed on the market. Physicians legally are permitted to prescribe approved drugs for uses that are not included in the product's labeling. However, drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label, and promotional claims

must be appropriately balanced with important safety information and otherwise be adequately substantiated. Failure to comply with these requirements can result in warning letters, adverse publicity, corrective advertising, and potential civil and criminal penalties.

Further, if there are any modifications to the drug, including changes in indications, labeling, or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new NDA or an NDA supplement, which may require the applicant to develop additional data or conduct additional nonclinical studies and clinical trials. As with new NDAs, the review process is often significantly extended by the FDA requests for additional information or clarification. Also, quality control and manufacturing procedures must continue to conform to cGMP requirements after approval to ensure and preserve the long-term identity, strength, quality, and purity of the drug product. The FDA periodically inspects manufacturing facilities to assess compliance with cGMP requirements, which imposes extensive procedural, substantive and record-keeping requirements. In addition, changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP requirements, and impose reporting and documentation requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP requirement and other aspects of regulatory compliance.

The testing and approval processes require substantial time, effort and financial resources, and each may take several years to complete. The FDA may not grant approval on a timely basis, or at all. Even if we believe a clinical trial has demonstrated safety and efficacy of one of our drug candidates for the treatment of a disease, the results may not be satisfactory to the FDA. Nonclinical and clinical data may be interpreted by the FDA in different ways, which could delay, limit or prevent regulatory approval. We may encounter difficulties or unanticipated costs in our efforts to secure necessary governmental approvals which could delay or preclude us from marketing drugs. The FDA may limit the indications for use or place other conditions on any approvals that could restrict the commercial application of the drugs.

Regulations Pertaining to Sales and Marketing

The marketing, distribution and sale of pharmaceutical products are subject to comprehensive governmental regulation both within and outside the United States.

Within the United States, numerous federal, state and local authorities have jurisdiction over, or enforce laws related to, such activities, including the FDA, Department of Health and Human Services, Centers for Medicare and Medicaid Services, Office of Inspector General, Department of Justice, and state Attorneys General.

We are subject to the FD&C Act and accompanying regulations that prohibit pharmaceutical companies from promoting a drug prior to approval from the FDA. If our product candidates receive marketing approval, we will also be subject to the prohibition on pharmaceutical companies promoting an approved drug in a manner inconsistent with the approved label. Similar laws and regulations exist outside of the United States.

We will be subject to various federal and state laws pertaining to health care “fraud and abuse,” including anti-kickback laws and false claims laws, for activities related to sales of any of our product candidates that may, in the future, receive 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 inform how the laws apply to particular industry practices. There is therefore a possibility that our practices might be challenged under such anti-kickback laws. In addition, there are federal and state false claims laws that prohibit anyone from knowingly and willingly presenting, or causing to be presented, any claims for payment for reimbursed drugs or services to third party payors (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).

In the United States, 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. These 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. In addition, several states require compliance with the Pharmaceutical Research and Manufacturers Association of America, or PhRMA, Code on Interactions with Healthcare Professionals, which further regulates pharmaceutical companies’ interactions with healthcare providers. Similarly, there are laws, regulations and industry codes, which will govern our activities outside of the United States, that restrict and govern pharmaceutical companies’ interactions with health care providers, and require disclosure of such interactions.

Pharmaceutical Pricing and Reimbursement

In both domestic and foreign markets, sales of any product candidates for which we receive regulatory approval for commercial sale will depend in part on the availability of reimbursement from third-party payors. Third-party payors include government authorities or programs, managed care providers, private health insurers and other organizations. These third-party payors are increasingly challenging the price and examining the cost-effectiveness of pharmaceutical products. In addition, significant uncertainty exists as to 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. Our product candidates may not be considered cost-effective. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

Within the United States, no uniform policy of coverage and reimbursement for drug products exists among third-party payors. If we obtain appropriate approval in the future to market any of our product candidates, those products could potentially be covered by various government health benefit programs and/or be purchased by government authorities. Participation in such programs or the sale of products to such agencies is subject to regulation. In order to participate in these programs, we may be required to provide discounted pricing or pay rebates on products paid for by government programs or purchasers or other third parties. Coverage of

pharmaceutical products by private health insurance varies. We may be required to provide scientific and clinical support for the use of our product candidates to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained. Private payers may also use a variety of utilization management techniques designed to control costs even for covered products. In addition, a private payer's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be provided. The marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and other third-party payors fail to provide adequate coverage and reimbursement.

The United States and state governments continue to propose and pass legislation designed 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, or the Healthcare Reform Act, substantially changed the way healthcare is financed by both governmental and private insurers. The law contains a number of provisions that affect coverage and reimbursement of drug products and/or that could potentially reduce the demand for pharmaceutical products such as:

- increasing drug rebates under state Medicaid programs for brand name prescription drugs and extending those rebates to Medicaid managed care;
- requiring drug manufacturers to provide a 50% discount on Medicare Part D brand name prescription drugs sold to Medicare beneficiaries whose prescription drug costs cause the beneficiaries to be subject to the Medicare Part D coverage gap (i.e., the so-called "donut hole").

Modifications to, or repeal of, all or certain provisions of the Healthcare Reform Act are expected as a result of the outcome of the recent presidential election and Republicans maintaining control of Congress, consistent with statements made by President Trump and members of Congress during the presidential campaign and following the election. 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, and we cannot predict how future federal or state legislative, judicial, or administrative changes relating to healthcare reform will affect our business.

Laws Relating to Foreign Trade

We are subject to various federal and foreign laws that govern our international business practices with respect to payments to government officials. Those laws include the U.S. Foreign Corrupt Practices Act, or FCPA, which prohibits U.S. companies and their representatives from paying, offering to pay, promising, or authorizing the payment of anything of value to any foreign government official, government staff member, political party, or political candidate for the purposes of obtaining or retaining business, or to otherwise obtain favorable treatment or influence a person working in an official capacity. In many countries, the health care professionals we regularly interact with may meet the FCPA's definition of a foreign government official. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect their transactions and to devise and maintain an adequate system of internal accounting controls.

In addition, the U.K. Bribery Act 2010, or Bribery Act, which proscribes giving and receiving bribes in the public and private sectors, bribing a foreign public official, and failing to have adequate procedures to prevent employees and other agents from giving bribes. U.S. companies that conduct business in the United Kingdom generally will be subject to the Bribery Act. Penalties under the Bribery Act include potentially unlimited fines for companies and criminal sanctions for corporate officers under certain circumstances.

There are local antibribery and anticorruption laws in countries where we are conducting clinical trials, such as Brazil, and Russia, and many of these also carry the risk of significant financial or criminal penalties. Finally, there are trade laws within the United States and outside that regulate the sale, purchase, import, export, reexport, transfer and

shipment of goods, products, materials, services and technology.

Other Regulations

We are also subject to numerous federal, state and local laws relating to such matters as safe working conditions, manufacturing practices, environmental protection, fire hazard control, and disposal of hazardous or potentially hazardous substances. We may incur significant costs to comply with such laws and regulations now or in the future.

Employees

As of December 31, 2016, we had 90 employees, 89 of whom were full-time, 18 of whom hold Ph.D. or M.D. degrees, 55 of whom were engaged in research and development activities and 35 of whom were engaged in business development, finance, information systems, facilities, human resources or administrative support. None of our employees are represented by any collective bargaining unit. We believe that we maintain good relations with our employees.

Facilities

Our corporate headquarters are located in Cambridge, Massachusetts. We currently lease approximately 45,362 square feet of office and lab space in Cambridge, Massachusetts, and sublease a small portion of that space (3,384 square feet). Excluding renewal options, the lease for the office space expires on September 11, 2026 and the lease for the lab space expires on November 30, 2021. We believe that our existing facilities are adequate to meet our current needs, and that suitable additional alternative spaces will be available in the future on commercially reasonable terms for our future growth.

Available Information

Our principal executive offices are located at 245 First Street, Cambridge, Massachusetts 02142. Our telephone number is (617) 871-2098. Our website address is www.akebia.com. The information found on our website, or that may be accessed by links on our website, is not part of this report. We make available, free of charge and through our Internet corporate website, our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and any amendments to any such reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, as soon as reasonably practicable after they are electronically filed with or furnished to the Securities and Exchange Commission.

Item 1A. Risk Factors

The following risk factors and other information included in this Annual Report on Form 10-K should be carefully considered. 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. Please reference our "Cautionary Note Regarding Forward-Looking Statements," which identifies certain forward-looking statements contained in this report that are qualified by these risk factors. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected.

Risks Related to our Financial Position and Need for Additional Capital

We have incurred significant losses since inception and anticipate that we will continue to incur significant losses for the foreseeable future and may never achieve or maintain profitability.

We have incurred net losses each year since our inception, including net losses of $135.7 million for the year ended December 31, 2016. As of December 31, 2016, we had an accumulated deficit of $297.1 million. To date, we have not commercialized any products or generated any revenue from the sale of products. We do not know whether or when we will generate revenue or become profitable.

We have devoted most of our financial resources to research and development, including our clinical and preclinical development activities. To date, we have financed our operations primarily through our public offerings of common stock, private placements of our preferred stock and strategic collaborations. The amount of our future net losses will depend, in part, on the rate of our future expenditures, and our financial position will depend, in part, on our ability to obtain funding through equity or debt financings or strategic collaborations. Even if we obtain regulatory approval to market vadadustat, our future revenue will depend upon the timing of such approval, the size of any markets in which vadadustat receives approval, our ability to achieve sufficient market acceptance, the availability and extent of reimbursement from third-party payors and other factors.

We expect to continue to incur significant expenses and increased operating losses for the foreseeable future. We anticipate that our expenses will increase significantly if and as we:

- conduct our Phase 3 development program of vadadustat for the treatment of anemia secondary to CKD, including the PRO_2TECT and $INNO_2VATE$ programs;
- develop plans for the preclinical and clinical development of AKB-5169 and AKB-6899;
- seek regulatory approvals for our product candidates that successfully complete clinical studies;
- have our product candidates manufactured for clinical trials and for commercial sale;
- establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval;
    - initiate additional preclinical, clinical or other studies for additional indications for vadadustat, AKB 6899, AKB-5169 and other product candidates that we may develop or acquire;
- seek to discover and develop additional product candidates;
- acquire, in-license and develop other commercial products, product candidates and technologies;
- make royalty, milestone or other payments under our agreement with Janssen and any future in-license agreements;
- maintain, protect and expand our intellectual property portfolio;
- attract and retain skilled personnel; and
- continue to create additional infrastructure to support our operations as a public company.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, if at all, we will be able to achieve profitability. If we are required by the FDA, EMA, or other regulatory authorities to perform studies in addition to,

different from or larger than those currently expected, or if there are any delays in completing our clinical trials or the development of any of our product candidates, our expenses could increase.

The net losses we incur may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance.

To become and remain profitable, we must succeed in developing and commercializing our product candidates, which must generate significant revenue. This will require us to be successful in a range of challenging activities, including completing preclinical testing and development and clinical trials of our product candidates, discovering or acquiring additional product candidates, obtaining regulatory approval for these product candidates and manufacturing, marketing and selling any products for which we may obtain regulatory approval. We are only in the preliminary stages of most of these activities. We may never succeed in these activities and, even if we do, may never generate revenue that is significant enough to achieve profitability.

We will require substantial additional financing. 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, 2016, our cash and cash equivalents and available for sale securities were $260.3 million. We believe that we will continue to expend substantial resources for the foreseeable future developing vadadustat, AKB-6899, AKB-5169 and any other product candidates that we may develop or acquire. These expenditures will include costs associated with research and development, potentially obtaining regulatory approvals and having our products manufactured, as well as marketing and selling products approved for sale, if any. In addition, other unanticipated costs may arise as a result of our decision to include certain elements in our programs. Because the outcome of our current and anticipated clinical trials is highly uncertain, we cannot reasonably estimate the actual amount of funding necessary to successfully complete the development and commercialization of our product candidates.

Our future capital requirements depend on many factors, including:

- significant costs associated with our Phase 3 clinical studies of vadadustat for the treatment of anemia secondary to CKD; we expect the cost of the Phase 3 program to be in the range of $80,000 to $85,000 per patient and the PRO_2TECT and $INNO_2VATE$ Phase 3 programs are designed to enroll approximately 5,700 CKD patients, aggregating in the range of $456.0 million to $484.5 million in external CRO costs for the total program; such estimated costs could increase significantly if the Phase 3 program takes longer to complete or if we choose to add additional investigative sites, add additional patients, modify the clinical trial protocol, or perform other studies in support of the Phase 3 program;
- the results of our meetings with the FDA and the EMA and other regulatory authorities and the consequential effect on study design, study size and resulting operating costs;
- difficulties or delays in enrolling patients in our clinical trials;
- assuming favorable Phase 3 clinical results, the timing of, and the costs involved in, obtaining regulatory approvals for vadadustat in dialysis and non-dialysis indications, including to fund the preparation and filing of regulatory submissions for vadadustat with the FDA, the EMA and other regulatory authorities, and whether we will seek regulatory approval for both indications simultaneously;
    - if Japanese subjects are not included in either $INNO_2VATE$ or PRO_2TECT, the amount of development funding received from our collaboration partner, MTPC, could differ materially;
- the cost, timing and outcome of our efforts to obtain marketing approval for vadadustat in the United States, Europe and in other jurisdictions;
- the scope, progress, results and costs of additional preclinical, clinical, or other studies for additional indications for vadadustat, as well as any studies of AKB-6899, AKB-5169 and other product candidates that we may develop or acquire;
- the timing of, and the costs involved in, obtaining regulatory approvals for AKB-6899, AKB-5169 and other product candidates that we may develop or acquire, if clinical studies are successful;
- the cost and timing of future commercialization activities for our products, if any of our product candidates are approved by regulatory authorities, including product manufacturing, marketing, sales and distribution costs;
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- the costs involved in preparing, filing and prosecuting patent applications and maintaining, defending and enforcing our intellectual property rights, including litigation costs, and the outcome of such litigation; and
- the extent to which we acquire or in-license other products, product candidates or technologies.

We ended 2016 with cash, cash equivalents and available for sale securities of $260.3 million and we expect these existing resources together with amounts expected to be received from Otsuka and MTPC, to fund our current operating plan into mid-2018. However, we currently estimate we will need additional funds to complete our Phase 3 development of vadadustat, including both the PRO2TECT and INNO2VATE clinical programs. We have based these estimates on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. We intend to secure a geographic collaboration for the development and commercialization of vadadustat in Europe and potentially other regions outside of the United States with a goal of

providing funds sufficient to enable us to complete our Phase 3 development of vadadustat, including both the PRO2TECT and INNO2VATE clinical programs. However, our development milestones may not be achieved, we may not receive the anticipated funding from our collaboration partner, we may not be able to secure another collaboration for the development and commercialization of vadadustat and we may not secure other sources of financing to complete our Phase 3 development of vadadustat.

We will require additional capital for the further development of our existing product candidates and will need to raise additional funds sooner to pursue development activities related to additional product candidates. If and until we can generate a sufficient amount of revenue from our products, we expect to finance future cash needs through public or private equity, debt offerings, or strategic transactions. Additional funds may not be available to us on acceptable terms or 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 product candidates. If we raise additional funds through the issuance of additional debt or equity securities, it could result in dilution to our existing stockholders or increased fixed payment obligations, and any such securities may have rights senior to those of our common stock. If we incur indebtedness, we could become subject to covenants that would restrict our operations and potentially impair our competitiveness, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. Any of these events could significantly harm our business, financial condition and prospects.

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

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings and license, development and commercialization agreements with collaborators. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of our common stockholders will be diluted, and the terms may include liquidation or other preferences and anti-dilution protections that adversely affect the rights of our common stockholders. 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 collaborations with third parties, we may have to relinquish valuable rights to our product candidates, future revenue streams, research programs or product 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 vadadustat, AKB 6899, AKB-5169 or any other product candidates that we develop or acquire, or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Risks Related to our Business and the Clinical Development, Regulatory Review and Approval of Vadadustat Other Product Candidates

We depend heavily on the success of one product candidate, vadadustat, which is in Phase 3 development. Even if we obtain favorable clinical results in our Phase 3 studies, we may not be able to obtain regulatory approval for, or successfully commercialize, vadadustat.

We currently have only one product candidate, vadadustat, in clinical development, and our business depends almost entirely on the successful clinical development, regulatory approval and commercialization of that product candidate, which may never occur. We currently have no drug products for sale, generate no revenue from sales of any drugs, and may never be able to develop marketable drug products. Vadadustat, which is in Phase 3 development, will require substantial additional clinical development, testing, manufacturing process development, and regulatory

approval before we are permitted to commence its commercialization. The clinical trials of our product candidates are, and the manufacturing and marketing of our product candidates will be, subject to extensive and rigorous review and regulation by numerous government authorities in the United States, Japan and in other countries where we intend to test and, if approved, market any product candidates. Before obtaining regulatory approval for the commercial sale of any product candidate, we must demonstrate through extensive preclinical testing and clinical trials that the product candidate is safe and effective for use in each target indication. This process can take many years. Of the large number of drugs in development in the United States, only a small percentage successfully complete the FDA regulatory approval process and are commercialized. Accordingly, even if we are able to obtain the requisite capital to continue to fund our development and clinical programs, we may be unable to successfully develop or commercialize vadadustat.

We are not permitted to market vadadustat in the United States until we receive approval from the FDA, or in any jurisdiction outside of the United States until we receive the requisite approval from regulatory authorities in such jurisdiction. MTPC, our collaboration partner in Asia, will not be permitted to market vadadustat in Japan without approval from the PMDA. As a condition to receiving

regulatory approval for vadadustat, we must complete Phase 3 studies and any additional non-clinical or clinical studies required by the FDA. Vadadustat may not be successful in clinical trials or receive regulatory approval. Further, vadadustat may not receive regulatory approval even if it is successful in clinical trials. Obtaining approval of an NDA in the United States is a complex, lengthy, expensive and uncertain process that typically takes many years following the completion of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, the safety concerns associated with injectable rESAs may affect the FDA's review of the safety results of compounds of this class, including vadadustat. Further, the policies or regulations, or the type and amount of clinical data necessary to gain approval, may change during the course of a product candidate's clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any product candidate and it is possible that vadadustat will never obtain regulatory approval. The FDA may delay, limit or deny approval of vadadustat for many reasons including, among others:

- we may not be able to demonstrate that vadadustat is safe and effective in treating anemia secondary to CKD to the satisfaction of the FDA;
- the results of our clinical trials may not meet the level of statistical or clinical significance required by the FDA for marketing approval;
- the FDA may disagree with the number, design, size, conduct or implementation of our clinical trials;
    - the FDA may not approve the formulation, labeling or specifications we request for vadadustat;
- the FDA may approve vadadustat for use only in a small patient population;
- the FDA may require that we conduct additional clinical trials;
- the contract research organizations, or CROs, that we retain to conduct our clinical trials may not perform effectively or take actions outside of our control that materially adversely impact our clinical trials;
- we or our contract manufacturers may fail to perform in accordance with the FDA's good clinical practice, or GCP, requirements;
- the FDA may disagree with inclusion of data obtained from certain regions outside the United States to support the NDA for potential reasons such as differences in clinical practice from United States standards;
- the FDA may disagree with our interpretation of data from our nonclinical studies and clinical trials;
- the FDA may not approve the manufacturing processes or facilities of third-party manufacturers with whom we contract; or
- the policies or regulations of the FDA may significantly change in a manner that renders our clinical data insufficient for approval, or requires us to amend or submit new clinical protocols.

In addition, similar reasons may cause the EMA or PMDA or other regulatory authorities to delay, limit or deny approval of vadadustat outside the United States.

We may find it difficult to enroll patients in our clinical studies, which could delay or prevent clinical studies of our product candidates.

Identifying and qualifying patients to participate in clinical studies of our product candidates is critical to our success. The timing of our clinical studies depends on the speed at which we can recruit patients to participate in testing our product candidates. Patients may be unwilling to participate in our clinical studies for vadadustat because of concerns from adverse events observed with injectable rESAs, other investigational agents and commercial products in CKD or for other reasons, including competitive clinical studies for similar patient populations. In addition, patients currently receiving treatment with injectable rESAs may be reluctant to participate in a clinical trial with an investigational drug. Finally, competition for clinical trial sites may limit our access to subjects appropriate for studies of vadadustat. As a result, the timeline for recruiting patients, conducting studies and obtaining regulatory approval of potential products may be delayed. These delays could result in increased costs, delays in advancing our development of vadadustat or termination of the clinical studies altogether.

We may not be able to identify, recruit and enroll a sufficient number of patients, or those with required or desired characteristics, to complete our clinical studies in a timely manner. Patient enrollment is affected by many factors, including:

- severity of the disease under investigation;
- design of the study protocol;

- size and nature of the patient population;
- eligibility criteria for, and design of, the study in question;
- perceived risks and benefits of the product candidate under study;
- proximity and availability of clinical study sites for prospective patients;
- availability of competing therapies and clinical studies and clinicians' and patients' perceptions as to the potential advantages of vadadustat in relation to available therapies or other products in development;
- efforts to facilitate timely enrollment in clinical studies;
- patient referral practices of physicians; and
- ability to monitor patients adequately during and after treatment.

We may not be able to initiate or continue clinical studies if we cannot enroll a sufficient number of eligible patients to participate in the clinical studies required by regulatory agencies. If we have difficulty enrolling a sufficient number of patients to conduct our clinical studies as planned, we may need to delay, limit or terminate on-going or planned clinical studies, any of which would have an adverse effect on our business.

We may not be able to conduct clinical trials in some jurisdictions outside of the United States.

We currently expect to seek regulatory approval of vadadustat for the treatment of anemia secondary to CKD in markets outside the United States, including the European Union and Japan. Our ability to successfully initiate, enroll and complete a clinical study in any country outside of the United States is subject to numerous risks unique to conducting business in international markets, including:

- difficulty in establishing or managing relationships with qualified CROs, physicians and clinical trial sites;
- different local standards for the conduct of clinical studies; and
- the potential burden of complying with a variety of laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatments.

Data obtained from studies conducted in the United States may not be accepted by the EMA and other regulatory authorities outside of the United States. Also, certain jurisdictions require data from studies conducted in their country in order to obtain approval in that country.

We are currently in discussions the Pharmaceuticals and Medical Devices Agency, or PMDA, in Japan regarding whether Japanese subjects may be enrolled in our global Phase 3 studies. The outcome of these discussions will have a significant impact on near-term payments that Mitsubishi Tanabe Pharma Corporation, or MTPC, will be obligated to make to us pursuant to our collaboration agreement with MTPC.

Once the results of certain Phase 2 studies of vadadustat in Japan are available, we and MTPC, following consultation with the PMDA, will determine whether a separate Phase 3 study of vadadustat will be required in Japan, which we refer to as the Local Scenario, or whether Japanese patients can take part in our global Phase 3 clinical studies, which we refer to as the Global Scenario. Under the Local Scenario, MTPC will be responsible for the costs of the local Phase 3 study in Japan and make no additional funding payments for the global Phase 3 program. In addition, $20.0 million of the $40.0 received in 2016 would be used to fund local development of vadadustat in Japan or be refunded to MTPC, at MTPC's discretion. This would reduce the total amount of upfront and development payments that we are eligible to receive under our agreement with MTPC from $100.0 million, to $20.0 million.

If we fail to successfully meet requirements for the conduct of clinical trials outside of the United States, we may be delayed in obtaining, or be unable to obtain, regulatory approval for vadadustat in countries outside of the United States.

Regulatory authorities outside of the United States will require compliance with numerous and varying requirements. The approval procedures vary among jurisdictions and may involve requirements for additional testing, and 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 drug product must be approved for reimbursement before it can be approved for sale in that country. In some cases, the price that we intend to charge for our drug product is also subject to approval. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside of the United States does not ensure approval by regulatory authorities in other countries or by the FDA. However, the failure to obtain approval in one jurisdiction may negatively impact our ability to obtain approval in another jurisdiction. The regulatory approval process in countries outside of the United States may include all of the

risks associated with obtaining FDA approval and, in some cases, additional risks. We may not obtain such regulatory approvals on a timely basis, if at all. We may not be able to file for regulatory approvals and may not receive the necessary approvals to commercialize our product candidates in any market. Also, favorable pricing in certain countries depends on a number of factors, some of which are outside the Company's control.

Clinical drug development is a lengthy and expensive process with an uncertain outcome, and positive results from the clinical studies of vadadustat thus far are not necessarily predictive of the results of any future clinical studies of vadadustat. If in our Phase 3 studies we cannot replicate the positive clinical results observed to date, we may be unable to successfully develop, obtain regulatory approval for and commercialize vadadustat.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. Success in preclinical studies may not be predictive of similar results in humans during clinical trials, and successful results from early or small clinical trials may not be replicated in later and larger clinical trials. For example, our encouraging preclinical and clinical results for vadadustat thus far do not ensure that the results of any future clinical trials will demonstrate similar results. Our vadadustat Phase 3 development program will enroll a larger number of subjects and will treat subjects for longer periods than our prior trials, which will result in a greater likelihood that adverse events may be observed. Many companies in the biopharmaceutical industry have suffered significant setbacks in late-stage clinical trials after achieving positive results in early stage development, and we may face similar setbacks. If the results of our ongoing or future clinical trials for vadadustat are inconclusive with respect to efficacy, if we do not meet our clinical endpoints with statistical significance, or if there are safety concerns or adverse events, we may be prevented from or delayed in obtaining marketing approval for vadadustat.

We could encounter delays if a clinical trial is suspended or terminated by us, by the relevant independent institutional review boards at the sites at which such trials are being conducted, by the Data Safety Monitoring Board, or DSMB, for such trial or by the FDA or other regulatory authorities. Such suspension or termination may be due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, critical findings resulting from inspection of clinical trial operations, clinical trial site or manufacturing facilities by the FDA or other regulatory authorities, the imposition of a clinical hold, unforeseen safety issues or adverse side effects, changes in laws or regulations, or lack of adequate funding to continue the clinical trial. Any delays in completing our clinical trials will increase our costs, slow down our product candidate development and approval process and jeopardize our ability to commence product sales and generate revenue. Any of these occurrences may harm our business, financial condition and prospects significantly.

Even if we receive regulatory approval for our product candidates, such products will be subject to ongoing regulatory review, which may result in significant additional expense. Additionally, our product candidates, if approved, could be subject to labeling and other restrictions, and we 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 receive for our product candidates may be subject to limitations on the approved indicated uses for which the product may be marketed or other conditions of approval, or contain requirements for potentially costly post-marketing studies and surveillance to monitor the safety and efficacy of the product. In addition, if the FDA approves any of our product 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, as well as continued compliance with current Good Manufacturing Practices, or cGMPs, and GCPs for any clinical trials that we conduct post-approval.

Post-approval discovery of previously unknown problems with an approved drug product, including adverse events of unanticipated severity or frequency or relating to 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 drug product, withdrawal of the drug product from the market, or drug product recalls;
- fines, warning letters or clinical holds;
- refusal by the FDA or other regulatory authorities to approve pending applications or supplements to approved applications filed by us, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products;
- a REMS program; and
- injunctions or the imposition of civil or criminal penalties.

The FDA's policies may change and additional government regulations may be enacted. 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 are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would adversely affect our business.

Risks Related to our Reliance on Third Parties

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

We are currently relying, and expect to continue to rely, on third parties, such as CROs, clinical data management organizations, medical institutions and clinical investigators, to conduct our current and future clinical trials, including our Phase 3 development program for vadadustat. We compete with many other companies for the resources of these third parties. The third parties on whom we rely may fail to perform effectively or terminate their engagement with us, and having to enter into alternative arrangements would delay development and commercialization of our product candidates.

We entered into an agreement with Quintiles, Inc. to be our primary CRO for the PRO_2TECT and $INNO_2VATE$ programs. If Quintiles cannot perform effectively or terminates their engagement with us, the progress of our Phase 3 clinical studies may be impacted and we may incur significant added costs in identifying, qualifying and contracting with a new CRO.

Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, the FDA and equivalent regulatory authorities outside of the United States require compliance with regulations and standards, including GCP requirements, for designing, conducting, monitoring, recording, analyzing and reporting the results of clinical trials to ensure that the data and results are credible and accurate and that the rights, integrity and confidentiality of study subjects are protected. Although we rely on third parties to conduct our clinical trials, we are responsible for ensuring that each of these clinical trials is conducted in accordance with its general investigational plan and protocol in compliance with legal and regulatory requirements. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs or clinical trial sites fail to comply with applicable GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, EMA or other regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP requirements. In addition, our clinical trials must be conducted with product that meets certain specifications and is manufactured under applicable cGMP regulations. Failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

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 regulatory requirements, or if they otherwise fail to comply with clinical trial protocols or meet expected deadlines, the clinical trials of our product candidates may not meet regulatory requirements. If clinical trials do not meet regulatory requirements or if these third parties need to be replaced, preclinical development activities or clinical trials may be extended, delayed, suspended or terminated. If any of these events occur, we may not be able to obtain regulatory approval of our product candidates on a timely basis or at all.

We also expect to rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our products, resulting in additional losses and depriving us of potential product revenue. In addition, we will be using an active comparator for our PRO_2TECT clinical program. If our distributors are unable to obtain sufficient supply of the active comparator for any reason, or supply active comparator to clinical trial sites in a timely manner, our clinical trials may be extended, delayed, suspended or terminated.

We rely on third parties to conduct some or all aspects of our product manufacturing, and these third parties may not perform satisfactorily.

We do not have any manufacturing facilities and do not expect to independently manufacture our product candidates for research and preclinical and clinical studies. We currently rely, and expect to continue to rely, on third parties to manufacture and supply drug product for our vadadustat clinical trials, and we expect to rely on third parties for the manufacture of clinical and commercial quantities of all of our product candidates. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

Also, these third parties may fail to perform effectively or terminate their engagement with us. We entered into an agreement with Evonik Corporation, or Evonik, for the manufacture of the drug substance for the Phase 3 development program of vadadustat. If Evonik cannot perform as agreed or terminates their engagement with us, we may be required to find replacement manufacturers. We may incur significant delays and added costs in identifying, qualifying and contracting with any such replacement, as well as producing the drug substance. We also have a Master Services Agreement with Esteve Quimica, or Esteve, to manufacture vadadustat for clinical trial use. We also have an agreement in place with Gregory Pharmaceutical Holdings (d/b/a UPM Pharmaceuticals Inc., or UPM) for the manufacture of finished drug product for the Phase 3 development program. Although we believe that there are several other manufacturers who also could manufacture our drug product if UPM cannot perform as agreed or terminates their engagement with us, we may incur significant delays and added costs in identifying, qualifying, and contracting with another manufacturer. Also, if we choose to engage a second source for the manufacture of drug product, we may incur additional costs. In addition, we have to enter into technology transfer agreements and share our know-how with such third-party manufacturers, which can be time-consuming and may result in delays. These delays could result in a suspension of our clinical trials or, if vadadustat is approved and marketed, a failure to satisfy patient demand.

Any of these events could lead to clinical study delays or failure to obtain regulatory approval, or affect our ability to successfully commercialize future products. Some of these events could be the basis for FDA action, including injunction, recall, seizure or total or partial suspension of production.

The facilities and processes used by our contract manufacturers to manufacture our product candidates will be inspected by the FDA and other regulatory authorities prior to or after we submit our marketing application. We do not control the manufacturing process of, and are completely dependent on, our contract manufacturers for compliance with cGMP requirements for manufacture of both drug substance and finished drug product. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and regulatory requirements, we will not be able to secure and/or maintain regulatory approval for our product candidates. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA, EMA or other regulatory authorities do not approve these facilities for the manufacture of our product candidates or if they withdraw any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved. Moreover, the failure of our contract manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect the supply of our products or product candidates.

In addition, our product candidates and any products that we may develop may compete with other product candidates and products for access to manufacturing facilities. Certain of these manufacturing facilities may be contractually prohibited from manufacturing our product candidates or products due to exclusivity provisions in agreements with our competitors. There are a limited number of manufacturers that operate under cGMP regulations and are capable of manufacturing for us.

If we are unable to obtain our product candidates in sufficient quantities and at sufficient yields, we may experience delays in product development, clinical trials, regulatory approval and commercial distribution.

Completion of our clinical trials and commercialization of our product candidates require access to facilities to manufacture our product candidates at sufficient yields and at clinical and commercial scale. We have limited experience manufacturing, or managing third parties in manufacturing, our product candidates in the volumes that will be necessary to support large-scale clinical trials or commercial sales. Our contractual manufacturers may not meet

initial expectations as to scheduling, scale-up, reproducibility, yield, purity, cost, potency or quality.

Our reliance on contract manufacturers may adversely affect our operations or result in unforeseen delays or other problems beyond our control. Because of contractual restraints and the limited number of contract manufacturers with the expertise, required regulatory approvals and facilities to manufacture our bulk drug substance and drug product on a commercial scale, replacement of a manufacturer may be expensive and time-consuming and may cause interruptions in the production of our product candidates. A contract manufacturer may also encounter difficulties in production.

Any delay or interruption in our supply of product candidates or products could have a material adverse effect on our business, financial condition, results of operations and cash flows.

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

We plan to co-commercialize vadadustat in the United States pursuant to our collaboration agreement with Otsuka and have entered into a collaboration agreement with MTPC to develop and commercialize vadadustat in Japan and certain other Asian countries. We will likely seek one or more strategic collaborators to commercialize vadadustat in additional markets. We face competition in seeking appropriate collaborators for our product candidates, and the negotiation process is time-consuming and complex. In order for us to successfully collaborate with third parties on our product candidates, potential collaborators must view these product candidates as economically valuable. Even if we are successful in our efforts to establish strategic collaborations, the terms that we agree upon may not be favorable to us, and we may not be able to maintain such strategic collaborations if, for example, development or approval of a product is delayed or sales of an approved product are disappointing. Any delay in entering into strategic collaboration agreements related to our product candidates could delay the development and commercialization of our product candidates and reduce their competitiveness even if they reach the market.

In addition, our strategic collaborators may terminate any agreements they enter into with us, and we may not be able to adequately protect our rights under these agreements. Furthermore, our strategic collaborators will likely negotiate for certain rights to control decisions regarding the development and commercialization of our product candidates, if approved, and may not conduct those activities in the same manner as we do.

If we fail to maintain our current collaboration with Otsuka or MTPC, or fail to enter into other strategic collaborations related to our product candidates, we will bear all of the risk and costs related to the development and commercialization of any such product candidate, and we may need to seek additional financing, hire additional employees and otherwise develop expertise. This could negatively affect the development and commercialization of any such product candidate.

Risks Related to our Intellectual Property

If our efforts to protect our proprietary technologies are not adequate, we may not be able to compete effectively in our market. We are currently involved in an opposition proceeding involving one of our European patents, and the outcome of that proceeding may affect our ability to establish a competitive advantage in the market or successfully commercialize our lead product candidate in the European Union.

We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our technologies. We will only be able to protect our product candidates, proprietary technologies and their uses from unauthorized use by third parties to the extent that valid and enforceable patents or trade secrets cover them. Any disclosure to or misappropriation by third parties of our confidential proprietary information could enable competitors to quickly duplicate or surpass our technological achievements, thus eroding our competitive position in the market.

In July 2011, a third party filed an opposition to one of our issued European patents, European Patent No. 2044005, or the ’005 Patent. During the oral proceedings, which took place on April 10, 2013, the Opposition Division of the European Patent Office decided to maintain certain claims of the patent directed to a compound chosen from a group of eight compounds, including vadadustat, as well as claims to compositions and methods for treating various diseases including, but not limited to, anemia. Both parties have appealed the decision of the Opposition Division and final resolution of the opposition proceeding will likely take a year or more. We cannot be assured of the breadth of the claims that will remain in the ’005 Patent or that the patent will not be revoked in its entirety. If the European Patent Office decides to narrow the scope of the claims or revoke the ’005 Patent, we may not be able to establish a competitive advantage in the European Union in our market or successfully commercialize our product candidates in the European Union, which could materially adversely affect our business, operating results and financial condition.

Composition-of-matter patents on the active pharmaceutical ingredient are generally considered to be the strongest form of intellectual property protection for pharmaceutical products, as such patents provide protection without regard to any method of use. Method-of-use patents protect the use of a product for the specified method. A method-of-use patent does not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their product for our targeted indications, physicians may prescribe these products “off-label.” Although off-label prescriptions may infringe or contribute to the infringement of method-of-use patents, the practice is common and such infringement is difficult to prevent or prosecute.

The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be uncertain. The patent applications that we own or license may fail to result in issued patents in the United States or in other countries. Our competitors have and we expect that they will continue to undertake formal efforts to oppose the issuance of claims in our patent applications. We do not control decisions made by the United States Patent and Trademark Office, or US PTO, or equivalent bodies outside the United States. Even if our patents do successfully issue, third parties may challenge the validity, enforceability, inventorship, or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property or prevent others

from designing around our claims. If the breadth or strength of protection provided by the patents and patent applications we hold with respect to our product candidates is threatened, it could dissuade companies from collaborating with us to develop, and threaten our ability to commercialize, our product candidates. Further, if we encounter delays in our clinical trials, the period of time during which we could market our product candidates under patent protection would be reduced. Since patent applications in the United States and most other countries are confidential for a period of time after filing, we cannot be certain that we were the first to file any patent application related to our product candidates. Furthermore, for applications in which all claims are entitled to a priority date before March 16, 2013, an interference proceeding can be provoked by a third-party or instituted by the US PTO to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. For applications containing a claim not entitled to priority before March 16, 2013, there is greater level of uncertainty in the patent law with the passage of the America Invents Act (2011), which brings into effect significant changes to the U.S. patent laws and which introduces new procedures for challenging pending patent applications and issued patents. A primary change under this reform is creating a “first to file” system in the United States. This will require us to be cognizant of the time from invention to filing of a patent application.

In addition to the protection afforded by patents, we seek to rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable, processes for which patents are difficult to enforce and any other elements of our drug discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. Although we require all of our employees to assign their inventions to us, and require all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information or technology to enter into confidentiality agreements, we cannot be certain that our trade secrets and other confidential or proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Furthermore, the laws of some countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. If we are unable to prevent unauthorized material disclosure of our intellectual property to third parties, we will not be able to establish or maintain a competitive advantage in the market, which could materially adversely affect our business, operating results and financial condition.

Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

Because we rely on third parties to research, develop and manufacture our product candidates, we must, at times, share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, services agreements, material transfer agreements, consulting agreements, research agreements or other similar agreements with our advisors, employees, third-party contractors and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, including our trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor’s discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business.

In addition, these agreements typically restrict the ability of our advisors, employees, third-party contractors and consultants to publish data potentially relating to our trade secrets, although our agreements may contain certain limited publication rights. For example, any academic institution that we may collaborate with will usually expect to be granted rights to publish data arising out of such collaboration. We often grant such rights, provided that we are

notified in advance and given the opportunity to delay publication for a limited time period in order for us to secure patent protection of intellectual property rights arising from the collaboration and remove confidential or trade secret information from any such publication. In the future, we may also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development or similar agreements. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of our agreements with third parties, independent development or publication of information by any of our third-party collaborators. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

Some of the intellectual property that protects our product candidates is owned by third parties and is licensed to us. Any dispute that might arise under any such license agreement could jeopardize our rights in such product candidates and materially harm our business.

We license intellectual property rights that protect some of our product candidates from third parties. If a dispute were to arise with a licensor pursuant to such a license agreement, our rights to use the licensed intellectual property and to develop and commercialize the compounds that such intellectual property covers could be jeopardized. If we have expended significant resources developing these compounds, such a dispute could have a material adverse effect on our business.

Third-party claims of intellectual property infringement may be costly and time consuming, and may delay or harm our drug discovery and development efforts.

Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of third parties. The pharmaceutical and biotechnology industries are characterized by extensive litigation over patent and other intellectual property rights. We have in the past and may in the future become a party to, or be threatened with, future adversarial litigation or other proceedings regarding intellectual property rights with respect to our drug candidates. As the pharmaceutical and biotechnology industries expand and more patents are issued, the risk increases that our drug candidates may give rise to claims of infringement of the patent rights of others.

While our product candidates are in preclinical studies and clinical trials, we believe that the use of our product candidates in these preclinical studies and clinical trials in the United States falls within the scope of the exemptions provided by 35 U.S.C. Section 271(e), which provides that it shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the United States a patented invention solely for uses reasonably related to the development and submission of information to the FDA. As our product candidates progress toward commercialization, the possibility of a patent infringement claim against us increases. We attempt to ensure that our product candidates and the methods we employ to manufacture them, as well as the methods for their use which we intend to promote, do not infringe other parties' patents and other proprietary rights. There can be no assurance they do not, however, and competitors or other parties may assert that we infringe their proprietary rights in any event.

Third parties may hold or obtain patents or other intellectual property rights and allege in the future that the use of our product candidates infringes these patents or intellectual property rights, or that we are employing their proprietary technology without authorization. We do not believe that there are any currently issued U.S. patents that conflict with our intellectual property rights; nor do we make any admission that any of such patents are valid, enforceable or infringed. Under U.S. law, a party may be able to patent a discovery of a new way to use a previously known compound, even if such compound itself is patented, provided the newly discovered use is novel and nonobvious. Such a method-of-use patent, however, if valid, only protects the use of a claimed compound for the specified methods claimed in the patent. This type of patent does not prevent persons from using the compound for any previously known use of the compound. Further, this type of patent does not prevent persons from making and marketing the compound for an indication that is outside the scope of the patented method. We are not aware of any valid U.S. patents issued to FibroGen, or any other person, that claim methods of using any of our product candidates for purposes of inhibiting hypoxia-inducible factor prolyl hydroxylases, or HIF-PHs, for the treatment of anemia secondary to CKD. For example, we are aware of certain patents that have been acquired by FibroGen directed to certain heterocyclic carboxamide compounds that are described as inhibitors of prolyl-4-hydroxylase. Those patents, however, are believed to have expired as of December 2014

FibroGen has also filed other patent applications in the U.S. and other countries directed to purportedly new methods of using such previously known heterocyclic carboxamide compounds for purposes of treating or affecting specified conditions, and some of these applications have since issued as patents. To the extent any such patents issue or have been issued, we may initiate opposition or other legal proceedings with respect to such patents. We have discussed the status of the opposition proceedings against FibroGen's European '823, '153,'155 and '333 patents below in Item 3. Legal Proceedings.

There may be other patents of FibroGen, or patents of third parties of which we are currently unaware with claims to compounds, materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our drug candidates. Also, because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our product candidates may infringe.

Third parties, including FibroGen, may in the future claim that our product candidates and other technologies infringe upon their patents and may challenge our ability to commercialize vadadustat. Parties making claims against us may seek and obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize vadadustat, AKB-6899 or other product candidates that we may develop or acquire. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our product candidates, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtained a license under the applicable patents, or until such patents expire or they are finally determined to be held invalid or unenforceable. Similarly, if any third-party patent were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or our intended methods of use, including patient selection methods, the holders of any such patent may be able to block or impair our ability to develop and commercialize the applicable product candidate unless we obtained a license or until such patent expires or is finally determined to be held invalid or unenforceable. We may also elect to enter into a license in order to settle litigation or in order to resolve disputes prior to litigation. Furthermore, even in the absence of litigation, we may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates. Should a license to a third-party patent become necessary, we cannot predict whether we would be able to obtain a license or, if a license were available, whether it would be available on commercially reasonable terms. If such a license is necessary and a license under the applicable patent is

unavailable on commercially reasonable terms, or at all, our ability to commercialize our product candidates may be impaired or delayed, which could in turn significantly harm our business.

Further, defense of infringement claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties or redesign our products, which may be impossible or require substantial time and monetary expenditure.

We are currently involved in opposition and invalidity proceedings and may in the future be involved in lawsuits or administrative proceedings to challenge the patents of our competitors or to protect or enforce our patents, which could be expensive, time consuming, and unsuccessful.

Competitors may infringe our patents or misappropriate our trade secrets or confidential information. To counter infringement or unauthorized use, we may be required to file infringement or misappropriation claims, which can be expensive and time-consuming. We may not be able to prevent infringement of our patents or misappropriation of our trade secrets or confidential information, particularly in countries where the laws may not protect those rights as fully as in the United States. In addition, in an infringement proceeding, a court may decide that a patent of ours is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated, held unenforceable, or interpreted narrowly and could put our patent applications at risk of not issuing. For example we are currently involved in five opposition proceedings in the European Patent Office. These proceedings may be ongoing for a number of years and may involve substantial expense and diversion of employee resources from our business. In addition, we may become involved in additional opposition proceedings or other legal or administrative proceedings in the future. For more information, see the other risk factors under "Risks Related to Intellectual Property" and Item 3 – Legal Proceedings.

In addition, there may be a challenge or dispute regarding inventorship or ownership of patents or applications currently identified as being owned by or licensed to us. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business.

Various administrative proceedings are also available for challenging patents, including interference, reexamination, inter partes review, and post-grant review proceedings before the US PTO or oppositions and other comparable proceedings in foreign jurisdictions. Interference proceedings provoked by third parties or brought by the US PTO may be necessary to determine the priority of inventions with respect to our patents or patent applications.

An unfavorable outcome in any current or future proceeding could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms or at all. Even if we are successful, participation in interference or other administrative proceedings before the US PTO or a foreign patent office may result in substantial costs and distract our management and other employees.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation and some administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees on any issued patent are due to be paid to the US PTO and foreign patent agencies in several stages over the lifetime of the patent. The US PTO and various foreign governmental patent agencies also require compliance with a number of procedural, documentary, fee payment (such as annuities) and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In such an event, our competitors might be able to enter the market, which would have a material adverse effect on our business.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties.

We have received confidential and proprietary information from potential collaborators, prospective licensees and other third parties. In addition, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies. We may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed confidential information of these third parties or our employees' former employers. We may also be subject to claims that former employees, collaborators or other third parties have an ownership interest in our patents or other intellectual property. We may be subject to ownership disputes in the future arising, for example, from conflicting obligations of consultants or others who are involved in developing our drug candidates. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against these claims, litigation could result in substantial cost and be a distraction to our management and employees.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on our product candidates in all countries throughout the world would be prohibitively expensive. Consequently, the breadth of our intellectual property rights in some countries outside the United States may be less extensive than those in the United States. In addition, the laws of some countries do not protect intellectual property rights to the same extent as laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other countries. Competitors may use our technologies in countries where we have not obtained patent protection to develop their own products and, further, may infringe our patents in territories where we have patent protection, but enforcement is not as strong as in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in certain countries. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property, particularly those relating to pharmaceutical and biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in countries outside of the United States could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Security breaches and unauthorized use of our IT systems and information, or the IT systems or information in the possession of our vendors, could damage the integrity of our clinical studies or compromise our ability to protect our intellectual property.

We are highly dependent on contract research organizations to carry out our clinical studies. A security breach, cyber-attack or unauthorized access of our clinical data could cause significant risk to our business, and could compromise our ability to protect our intellectual property. Cyber-attacks can include malware, computer viruses, hacking or other significant compromise of our computer, communications and related systems. Although we take

steps to manage and avoid these risks and to be prepared to respond to attacks, our preventive and any remedial actions may not be successful. Likewise, although we believe our vendors and service providers take steps to manage and avoid information security risks and respond to attacks, we may be vulnerable to attacks against our vendors or service providers, and we may not have adequate contractual remedies against such vendors and service providers in such event. Such attacks, whether successful or unsuccessful, could result in our incurring costs related to, for example, rebuilding internal systems, defending against litigation, responding to regulatory inquiries or actions, paying damages or fines, or taking other remedial steps with respect to third parties. Publicity about vulnerabilities and attempted or successful incursions could damage the integrity of our studies or delay their completion. In addition, such attacks could compromise our ability to protect our trade secrets and proprietary information from unauthorized access or misappropriation.

Risks Related to Commercialization

Our future commercial success depends upon attaining significant market acceptance of our product candidates, if approved, among physicians, patients, third-party payors and others in the medical community.

Even if we obtain marketing approval for vadadustat, AKB-6899, AKB-5169 or any other product candidates that we may develop or acquire in the future, these product candidates may not gain market acceptance among physicians, third-party payors, patients and

others in the medical community in the United States or in other countries. In addition, market acceptance of any approved products depends on a number of other factors, including:

- the safety and efficacy of the product, as demonstrated in clinical trials, and in the post-marketing setting;
- the prevalence of the disease treated by our product;
- the clinical indications for which the product is approved and the product label approved by regulatory authorities, including any warnings or limitations that may be required on the label or as a consequence of potential safety risks associated with the product;
- the claims we are able to make regarding the safety and efficacy of our products;
- acceptance by physicians and patients of the product as a safe and effective treatment and the willingness of the target patient population to try new therapies and of physicians to prescribe new therapies;
- the cost, safety and efficacy of the product in relation to alternative treatments;
- the timing of product launch relative to competing products;
- the availability of adequate coverage and reimbursement by third-party payors and governmental authorities;
- relative convenience and ease of administration;
- the prevalence and severity of adverse side effects;
- the effectiveness of our sales and marketing efforts; and
- the restrictions on the use of our products together with other medications, if any.

Market acceptance of any of our product candidates, if approved, may also depend on factors specific to such candidates, such as our ability to contract with dialysis providers. Two of the largest operators of dialysis clinics in the United States, DaVita, Inc., or DaVita, and Fresenius Medical Care, or Fresenius, account for more than half of the injectable rESA sales in the U.S. dialysis market. We believe that it may be challenging to enter into supply agreements with DaVita, Fresenius or other operators of dialysis clinics.

Market acceptance is critical to our ability to generate significant revenue. In addition, any product 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.

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

Undesirable side effects caused by our products or even competing products in development that utilize a common mechanism of action could cause us 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 could lead to potential product liability claims. In our Phase 2b study of vadadustat for the treatment of anemia secondary to CKD in patients not on dialysis, the incidence of the most common treatment emergent adverse events were well balanced overall between the vadadustat and placebo treatment groups. There was a higher incidence of serious adverse events (SAEs) reported in the vadadustat treatment group, the most common being renal-related. The disparity in renal SAE’s was likely related to variability in reporting between investigators.

The patients in our clinical studies have CKD, a serious disease that increases the risk of cardiovascular disease including heart attacks and stroke, and, ultimately may cause kidney failure. Many of patients with CKD are elderly with comorbidities making them susceptible to significant health risks. Therefore, the likelihood of these patients having adverse events, including serious adverse events, while participating in our studies is high.

Serious adverse events deemed to be possibly or probably related to vadadustat could have a material adverse effect on the development of our product candidates and our business as a whole. Our understanding of adverse events in future clinical trials of our product candidates may change as we gather more information, and additional unexpected

adverse events may be observed in future clinical trials.

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

- our clinical trials may be put on hold;
- patient recruitment could be slowed, and enrolled patients may not want to complete the clinical trial;
- we may be unable to obtain regulatory approval for our product candidates or regulatory authorities may withdraw approvals of product candidates;
- regulatory authorities may require additional warnings on the label;
- a medication guide outlining the risks of such side effects for distribution to patients may be required;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

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

If we are unable to establish sales, marketing and distribution capabilities or to enter into additional agreements with third parties to market and sell our product candidates, we may not be successful in commercializing our product candidates if and when they are approved.

We are currently collaborating with Otsuka to develop and commercialize vadadustat in the United States, and MTPC to develop and commercialize vadadustat in Japan. We do not have a sales or marketing infrastructure and we have not yet sold, marketed or distributed any of our products. To achieve commercial success for any product for which we obtain marketing approval, we will need to establish a sales and marketing organization or make arrangements for sales and marketing services, either by establishing our own or entering into additional geographic collaborations.

There are risks involved with establishing our own sales, marketing and distribution capabilities. For example, recruiting and training a sales force are expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

If we are unable to establish our own sales, marketing and distribution capabilities and have to enter into arrangements with third parties to perform these services, our profitability, if any, is likely to be lower than if we were to market, sell and distribute any products that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell, market and distribute our product candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

We have entered into collaboration agreements with Otsuka Pharmaceutical Co. Ltd. and MTPC pursuant to which we granted to Otsuka the co-exclusive right to develop and commercialize vadadustat in the United States and granted MTPC the exclusive right to develop and commercialize vadadustat in Japan and other Asian countries, each of which is key to our success. If either Otsuka or MTPC fails to perform under these agreements, our future results could be materially harmed.

In addition to certain substantial upfront payments and development milestones, our agreement with Otsuka establishes a profit sharing arrangement for the commercialization of vadadustat in the United States, in which we and Otsuka equally share the costs of developing and commercializing vadadustat in the United States and profits from the sales of vadadustat after approval by the FDA. Similarly, our agreement with MPTPC grants them the exclusive right to develop and commercialize vadadustat in Japan and certain Asian countries in exchange for upfront, milestone, and royalty payments. We partnered with each company, in part, because they have a well-established commercial presence and infrastructure in their territories, and we expect them to help us prepare for and execute on an optimal launch of vadadustat in those geographies. If either of these companies fails to perform their obligations diligently under their agreement with us, including failing to diligently commercialize vadadustat in their territories, our sales potential in the United States and Japan may be materially harmed and we may not have an adequate remedy for such harm under our agreements with either company. Furthermore, if a contractual dispute with either Otsuka or MTPC were to arise, it could result in costly litigation for the Company and jeopardize important revenue streams, which could materially harm our financial condition.

Coverage and reimbursement may be limited or unavailable in certain market segments for our products, if approved, which could make it difficult for us to sell our products profitably.

Market acceptance and sales of any approved products will depend significantly on the availability of adequate coverage and reimbursement from third-party payors and may be affected by existing and future healthcare reform measures. Government authorities and third-party payors decide which drugs they will cover, establish formularies, or implement other mechanisms to manage utilization of products, and determine reimbursement levels. Coverage and reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient; and
- cost-effective.

Obtaining coverage and reimbursement approval for a product from a government or other third-party payor 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 payor. Additionally, we may be required to enter into contracts with third-party payors offering rebates on our products in order to obtain favorable formulary status. We may not be able to agree upon commercially reasonable terms with such third-party payors or provide data sufficient to obtain favorable coverage and reimbursement. We cannot be sure that coverage or adequate reimbursement will be available for any of our product candidates. Even if we obtain coverage for our product candidates, third-party payors may not establish adequate reimbursement amounts, which may reduce the demand for our product, and prompt us to have to reduce pricing for the products. If reimbursement is not available or limited, we may not be able to commercialize certain of our products. In addition, in the United States third-party payors 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 reimbursement third-party payors will provide for newly approved drugs, which in turn will put pressure on the pricing of drugs.

In addition, if vadadustat is used in an outpatient dialysis facility, such facilities often receive fixed reimbursement for a bundle of dialysis services, including certain drugs and supplies used to treat patients with end-stage renal disease, or ESRD. For example, Medicare payments to ESRD facilities for dialysis treatments are based on a prospective payment system with a standard per treatment payment (subject to certain adjustments such as patient level-case-mix adjustment). The per treatment payment covers a bundle of items and services routinely required for dialysis treatments furnished to Medicare beneficiaries in Medicare-certified ESRD facilities or at home, including the cost of certain routine drugs. At this time, we believe that vadadustat, if approved, will likely be included in the bundle. We may be unable to sell vadadustat, if approved, to dialysis providers on a profitable basis if third-party payors reduce their current levels of payment or if our costs of production increase faster than increases in reimbursement levels. Patient and provider access to adequate coverage and reimbursement by government and private insurance plans is central to the acceptance of any products for which we receive regulatory approval.

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

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

reduce prices, and even, in some instances, render commercialization in a market infeasible or disadvantageous from a financial perspective. In some countries, we may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our product candidates to other available products in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third-party payors or government authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be adversely affected.

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

Our revenue prospects could be affected by changes in healthcare spending and policy in the United States and abroad. We operate in a highly regulated industry and new laws, regulations or judicial decisions, or new interpretations of existing laws or, regulations

related to healthcare availability or the method of delivery or payment for healthcare products and services could negatively impact our business, operations and financial condition.

The U.S. healthcare industry generally and U.S. government healthcare programs in particular are highly regulated and subject to frequent and substantial changes. For example, in 2010, and as described above, the Healthcare Reform Act, which represented one of the most significant healthcare reform measures in decades, was enacted. Modifications to or repeal of all or certain provisions of the Healthcare Reform Act are expected as a result of the outcome of the recent presidential election and Republicans maintaining control of Congress, consistent with statements made by Donald Trump and members of Congress during the presidential campaign and following the election. The full impact on our business of the Healthcare Reform Act or its potential future repeal or amendment is uncertain.

Federal and state legislatures within the United States and governments in other countries will likely continue to consider changes to existing healthcare legislation, and, in particular, we anticipate additional governmental reforms intended to control drug costs. We cannot predict the reform initiatives that may be adopted in the future. Private health plans may also increase efforts to manage utilization and control drug costs. The continuing efforts of the government or private third party payors of to contain or reduce costs of healthcare may adversely affect:

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

Even prior to approval, we are subject to a complex regulatory scheme that requires Company resources to ensure compliance. Failure to comply with applicable laws could subject the Company to government scrutiny or government enforcement, potentially resulting in costly investigations and/or fines or sanctions, or impacting our relationship with key regulatory agencies such as FDA or EMA.

Even before we have obtained approval for vadadustat or any product, certain laws apply to the Company or may otherwise restrict its activities, including the following:

- United States federal securities laws restricting the purchase or sale of any securities while in possession of material, non-public information;
- laws and regulations governing the conduct of clinical and preclinical studies in the United States and in countries in which we are conducting such studies;
- laws and regulations in the United States and in countries in which we are interacting with health care providers, patients, patient organizations and other constituencies that prohibit promoting a drug prior to approval and/or reimbursement;
- laws, regulations and industry codes that vary from country to country and govern Akebia's relationships with health care providers, patients, patient organizations, and other constituencies, and prohibit certain types of gifts and entertainment, establish codes of conduct, and in some instances, require disclosure to, or approval by, regulatory authorities for Akebia to engage in arrangements with such constituencies;
- anti-corruption and anti-bribery laws, including the FCPA and various other anti-corruption laws in countries outside of the United States. The FCPA generally prohibits companies and their intermediaries, such as the CROs, contract manufacturing organizations, and distributors with which we do business outside the United States from making improper payments to foreign officials for the purposes of obtaining or keeping business and/or other benefits;
- data privacy laws existing in the European Union and other countries in which we operate, including the United States' federal Health Insurance Portability and Accountability Act of 1996 (HIPAA), as amended by the Health Information Technology for Economic and Clinical Health Act (HITECH), and state privacy and data protection laws, as well as state consumer protection laws; and

- international trade laws, which are laws that regulate the sale, purchase, import, export, re-export, transfer and shipment of goods, products, materials, services and technology.

If our product candidates obtain marketing approval, we will be subject to healthcare laws, regulation and enforcement and our failure to comply with those laws could have a material adverse effect on our results of operations and financial conditions.

If we obtain approval for any of our product candidates and begin commercializing them, our operations may be directly, or indirectly through our customers, subject to additional healthcare regulation and enforcement by the federal government, states and governments outside of the United States in which we conduct our business. In addition to the laws mentioned above, the laws that may affect our ability to operate include:

- the FD&C Act, which among other things, strictly regulates drug product marketing, prohibits manufacturers from marketing such products for off-label use and regulates the distribution of samples;
- the federal anti-kickback law, which prohibits, among other things, persons from soliciting, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual, for an item or service or the purchasing or ordering of a good or service, for which payment may be made under federal healthcare programs such as Medicare and Medicaid;
- federal false claims laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, information or claims for payment from Medicare, Medicaid, or other third-party payers that are false or fraudulent;
- federal laws that require pharmaceutical manufacturers to report certain calculated product prices to the government or provide certain discounts or rebates to government authorities or private entities, often as a condition of reimbursement under a government healthcare programs;
- the so-called "federal sunshine" law (also known as "open payments") which requires pharmaceutical and medical device manufacturers to report certain financial interactions to the federal government for re-disclosure to the public;
- the federal HIPAA, which, in addition to privacy protections, prohibits executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- state law equivalents of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payer, including commercial insurers, and state transparency laws, many of which state laws differ from each other in significant ways and often are not preempted by federal laws, thus complicating compliance efforts; and
- state laws restricting interactions with healthcare providers and other members of the healthcare community or requiring pharmaceutical manufacturers to implement certain compliance standards.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. In addition, recent healthcare reforms have strengthened these laws. For example, the Healthcare Reform Act, among other things, amended the intent requirement of the federal anti-kickback law. A person or entity no longer needs to have actual knowledge of the statute or specific intent to violate the law. The Healthcare Reform Act also amended the False Claims Act, such that violations of the anti-kickback statute are now deemed violations of the False Claims Act.

If our operations are found to be in violation of any of such laws or any other governmental regulations that apply to us, we may be subject to, on a corporate or individual basis, penalties, including civil and criminal penalties, damages, fines, the curtailment or restructuring of our operations, the exclusion from participation in federal and state healthcare programs and even imprisonment, any of which could materially adversely affect our ability to operate our business and our financial results. In addition, the cost of implementing sufficient systems, controls, and processes to ensure compliance with all of the aforementioned laws could be significant.

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

The development and commercialization of new drug products is highly competitive. Our future success depends on our ability to demonstrate and maintain a competitive advantage with respect to the development and commercialization of our product candidates. Our objective is to develop and commercialize new products with superior efficacy, convenience, tolerability and/or safety. In many cases, the products that we commercialize will compete with existing, market-leading products.

If vadadustat is approved and launched commercially, competing drugs may include EPOGEN® and Aranesp®, commercialized by Amgen, Procrit® and Eprex®, commercialized by Johnson & Johnson, and Mircera®, commercialized by Roche Holding Ltd., or Roche. We may face competition from potential new anemia therapies. There are several other HIF product candidates in various

stages of active development for anemia indications that may be in direct competition with vadadustat if and when they are approved and launched commercially. These candidates are being developed by such companies as FibroGen, in collaboration with AstraZeneca PLC in the United States and China and with Astellas Pharma Inc. in Europe and Asia, Japan Tobacco International, GlaxoSmithKline plc and Bayer HealthCare AG. FibroGen is currently in Phase 3 clinical development of its product candidate, roxadustat, and GlaxoSmithKline plc recently commenced Phase 3 studies of its product candidate, daprodustat. Some of these product candidates may enter the market as early as 2017. In addition, certain companies are developing potential new therapies for renal-related diseases that could potentially reduce rESA utilization and thus limit the market for vadadustat if and when it is approved and launched commercially. Other new therapies are in development for the treatment of conditions inclusive of renal anemia, like sotatercept from Acceleron Pharma Inc., that may impact the market for anemia-targeted treatment.

Since rESAs are biologic products, the introduction of biosimilars into the rESA market in the United States will constitute additional competition for vadadustat if we are able to obtain approval for and commercially launch our product. A biosimilar product is a follow-on version of an existing, branded biologic product. The patents for the existing, branded product must expire in a given market before biosimilars may enter that market without risk of being sued for patent infringement. In addition, an application for a biosimilar product cannot be approved by the FDA until 12 years after the existing, branded product was approved under a Biologics License Application, or BLA. The patents for epoetin alfa, an rESA, expired in 2004 in the European Union, and the remaining patents expired between 2012 and 2015 in the United States. Several biosimilar versions of rESAs are available for sale in the European Union and biosimilar versions of rESAs are currently being studied in clinical trials in the United States.

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 manufacturing pharmaceutical products. Large and established companies such as Amgen and Roche, among others, compete in the market for drug products to treat anemia. In particular, these companies have greater experience and expertise in conducting pre-clinical testing and clinical trials, obtaining regulatory approvals to market products, manufacturing such products on a broad scale and marketing approved 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 product 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 competitive products before, or more effectively than, we do. If we are not able to compete effectively against potential competitors, our business will not grow and our financial condition and operations will suffer.

Risks Related to our Business and Industry

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

Recruiting and retaining qualified scientific, clinical, medical, manufacturing and sales and marketing personnel will also be critical to our success. We are highly dependent on certain members of our senior management. The loss of the services of our executives, senior managers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executives and other key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products. We may be unable to hire,

train, retain or motivate these key personnel on acceptable terms given the intense competition among numerous biopharmaceutical companies for similar personnel.

We also experience competition for the hiring of 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 become employed by companies other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to grow and pursue our business strategy will be limited.

Our employees, independent contractors, principal investigators, CROs, consultants and vendors may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading.

We are exposed to the risk that our employees, independent contractors, principal investigators, CROs, consultants and vendors may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or unauthorized activities that violate applicable laws, including (1) FDA and other healthcare authorities' regulations,

including those laws that require the reporting of true, complete and accurate information to regulatory authorities, and those prohibiting the promotion of unapproved drugs or approved drugs for an unapproved use, (2) quality standards, including Good Laboratory Practices (GLP), GCP and GMP, (3) federal and state healthcare fraud and abuse laws and regulations, (4) anti-bribery and anti-corruption laws, such as the FCPA, that prohibit the making of improper payments to foreign officials for the purposes of obtaining any business advantage, (5) laws that require the reporting of true and accurate financial information and data, and (6) securities laws and regulations. Specifically, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. It is not always possible to identify and deter misconduct by employees and third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, or if any such action is instituted against our employees, consultants, vendors or principal investigators, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, curtailment of our operations, and imprisonment, any of which could adversely affect our ability to operate our business and our results of operations.

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

As we seek to advance our product candidates through clinical trials and commercialization, we will need to expand our clinical, medical, regulatory, manufacturing, marketing and sales capabilities or contract with third parties to provide these capabilities for us. We have recently entered into a number of strategic collaborations for the development and commercialization of vadadustat. As our operations expand, we expect that we will need to manage additional relationships with various strategic collaborators, 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 vadadustat, if approved, and any other product 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, integrate and retain additional 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 product candidates.

We face an inherent risk of product liability as a result of the clinical testing of our product 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 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 product candidates. Even a successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, product liability claims may result in:

- decreased demand for any product candidates or products that we may develop;
- injury to our reputation and significant negative media attention;

- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to study participants or patients;
- product recalls or withdrawals, or labeling, marketing or promotional restrictions;
- loss of revenue;
- the inability to commercialize any product candidates that we may develop; 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 that we believe is appropriate for our stage of development and may need to obtain higher levels prior to marketing any of our product candidates. Although we maintain product liability insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the use and disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from the use of hazardous materials by our employees or consultants, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Risks Related to our Common Stock

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012. As a result, we intend to continue to take advantage of certain reduced disclosure requirements.

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and obtaining shareholder approval of any golden parachute payments not previously approved.

Investors may find our common stock less attractive if we continue to rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile. In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of these accounting standards until they would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

We could be an emerging growth company for up to five years from our initial public offering in March 2014, although circumstances could cause us to lose that status earlier, including (1) if the market value of our common stock held by non-affiliates exceeds $700 million as of any June 30 before that time or (2) if we have total annual gross revenue of $1 billion or more during any fiscal year before that time, in which cases we would no longer be an emerging growth company as of the following December 31, or (3) if we issue more than $1 billion in non-convertible debt during any three-year period before that time, we would cease to be an emerging growth company immediately.

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

Our stock price has been and may continue to be volatile. Since our initial public offering in March 2014, the price of our common stock as reported on The NASDAQ Global Market has ranged from a low of $5.91 on August 25, 2015 to a high of $31.00 on June 20, 2014. The market price of shares of our common stock could be subject to wide fluctuations in response to many risk factors listed in this section, and others beyond our control.

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 the factors listed above to the extent that they affect our industry, markets or products. In the past, securities class action litigation has often been initiated against companies following periods of volatility in their stock price, and such an action has been filed against us. 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.

Provisions in our charter documents 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.

Provisions in our Amended and Restated Certificate of Incorporation and Amended and Restated By-Laws contain provisions that may have the effect of discouraging, delaying or preventing a change in control of us or changes in our management. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our Board of Directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our Board of Directors. Among other things, these provisions:

- 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 pursuant to a resolution adopted by a majority of the total number 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;
- 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;
- require a supermajority vote of the holders of our common stock or the majority vote of our Board of Directors to amend our Amended and Restated By-Laws; and
- require a supermajority vote of the holders of our common stock to amend the classification of our Board of Directors into three classes and to amend certain other provisions of our Amended and Restated Certificate of Incorporation.

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

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

Any provision of our Amended and Restated Certificate of Incorporation, our 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 ability to use net operating losses to offset future taxable income may be subject to certain limitations.

In general, under Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, a corporation that undergoes an "ownership change" is subject to limitations on its ability to utilize its pre-change net operating losses, or NOLs, to offset future taxable income. Our existing NOLs may be subject to substantial limitations arising from previous ownership changes and our ability to utilize NOLs could be further limited by Section 382 of the Code. Future changes in our stock ownership, many of which are outside of our control, could result in an ownership change under Section 382 of the Code. Our NOLs may also be impaired under state law. Accordingly, we may not be able to utilize a material portion of our NOLs. Furthermore, our ability to utilize our NOLs is conditioned upon our attaining profitability and generating U.S. federal taxable income. As described above under "—Risks related to our financial position and need for additional capital," we have incurred significant net losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future; thus, we do not know whether or when we will generate the U.S. federal taxable income necessary to utilize our NOLs. A full valuation allowance has been provided for the entire amount of our NOLs.

Our Amended and Restated Certificate of Incorporation designates the state or federal courts located in the State of Delaware as the sole and 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 Amended and Restated Certificate of Incorporation provides that, subject to limited exceptions, the state and federal courts located in the State of Delaware will be the sole and exclusive forum 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 Amended and 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 Amended and 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 Amended and Restated Certificate of Incorporation inapplicable to, or unenforceable with respect to, 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.

Item 1B. Unresolved Staff Comments
None

Item 2. Properties

Our corporate headquarters are located in Cambridge, Massachusetts. We currently lease approximately 45,362 square feet of office and lab space in Cambridge, Massachusetts and sublease a small portion of that space (3,384 square feet). Excluding renewal options, the lease for the office space expires on September 11, 2026 and the lease for the lab space expires on November 30, 2021. We believe that our existing facilities are adequate to meet our current needs, and that suitable additional alternative spaces will be available in the future on commercially reasonable terms for our future growth.

Item 3. Legal Proceedings

Shareholder Litigation

In September 2015, a purported securities class action lawsuit was filed against us, including our Chief Executive Officer, our Chief Financial Officer, and members of our Board of Directors, in the Business Litigation Section of the Suffolk County Superior Court of Massachusetts. The complaint is brought on behalf of an alleged class of those who purchased our common stock pursuant or traceable to our initial public offering, and purports to allege claims arising under Sections 11, 12(a)(2) and 15 of the Securities Act of 1933, as amended. The complaint generally alleges that the defendants violated the federal securities laws by, among other things, making material misstatements or omissions concerning the Phase 2b clinical study of vadadustat. The complaint seeks, among other relief, unspecified compensatory damages, rescission of certain stock purchases, attorneys' fees, and costs. In October 2015, we removed the case to the United States District Court for the District of Massachusetts, and the plaintiff filed a motion to remand the case back to the Business Litigation Section of the Suffolk County Superior Court of Massachusetts. The plaintiff's motion to remand was granted in April 2016. The plaintiff filed an amended complaint in the Suffolk County Superior Court on August 15, 2016, and we served our memorandum in support of our motion to dismiss the amended complaint on October 14, 2016. The motion to dismiss

hearing was held on January 31, 2017. The Court granted our motion to dismiss and dismissed the case with prejudice on February 21, 2017. The plaintiff has 30 days to appeal the decision. We believe such claims are without merit and we will engage in a vigorous defense of such appeal, if it is ultimately filed by the plaintiff.

Opposition Proceeding Against Our ’005 Patent

In July 2011, a third party filed an opposition to our issued European Patent No. 2044005, or the ’005 Patent. During the oral proceedings, which took place on April 10, 2013, the Opposition Division of the European Patent Office maintained the ’005 Patent on the basis of the third auxiliary request filed during the oral proceedings. This decision resulted in the maintenance of a claim directed to a compound chosen from a group of eight compounds, including vadadustat, as well as claims to compositions and methods for treating various diseases, including, but not limited to, anemia. Both parties have appealed the decision of the Opposition Division and final resolution of the opposition proceedings will likely take a year or more. We cannot be assured of the breadth of the claims that will remain in the ’005 Patent or that the patent will not be revoked in its entirety.

Opposition and Invalidity Proceedings Against FibroGen Inc.

We have had a number of positive developments in our opposition and invalidity proceedings against FibroGen, Inc., or FibroGen. With regard to the opposition that we filed in Europe against FibroGen’s European Patent No. 1463823, or the ’823 patent, an oral proceeding took place March 8 and 9, 2016. Following the oral proceeding, the European Opposition Division ruled that the patent as granted did not meet the requirements for patentability under the European Patent Convention and, therefore, revoked the patent in its entirety. FibroGen has appealed that decision and the appeal process is expected to take 2 – 3 years. Likewise, with regard to the invalidity proceeding that we filed in Japan against certain claims of FibroGen’s Japanese Patent No. 4804131, or the ’131 patent, which is the Japanese counterpart to the ’823 patent, the Japan Patent Office, or JPO, issued a preliminary decision finding all of the challenged claims to be invalid. FibroGen subsequently amended the claims and the JPO accepted the amendments. The resulting FibroGen Japanese ’131 patent does not cover vadadustat or any pyridine carboxamide compounds. To date, FibroGen has been unsuccessful in its attempts to obtain a patent in the United States covering the same claim scope as it obtained initially in Europe and Japan in the ’823 and ’131 patents. In the event FibroGen were to obtain such a patent in the United States, we may decide to challenge the patent like we have done in Europe and Japan.

On May 13, 2015, May 20, 2015 and July 6, 2015 we filed oppositions to FibroGen’s European Patent Nos. 2322153, 2322155, and 163333, or the ’153 patent, the ’155 patent, and the ’333 patent, respectively, requesting the patents be revoked in their entirety. These related patents claim, among other things, various compounds that either stabilize HIF or inhibit a HIF hydroxylase or a HIF prolyl hydroxylase for treating or preventing various conditions, including, inter alia, iron deficiency, microcytosis associated with iron deficiency, anemia of chronic disease, anemia wherein the subject has a transferrin saturation of less than 20%, anemia refractory to treatment with exogenously administered erythropoietin, or EPO, and microcytosis in microcytic anemia. Such method of use patents do not prevent persons from using the compound for other uses, including any previously known use of the compound. In particular, these patents do not claim methods of using any of our product candidates for purposes of inhibiting hypoxia-inducible factor prolyl hydroxylases, or HIF-PHs, for the treatment of anemia secondary to CKD. While we do not believe these patents will prevent us from commercializing vadadustat for the treatment of anemia secondary to CKD, we filed these oppositions to provide us and any future partners with maximum flexibility for developing vadadustat and our pipeline of HIF PH inhibitors. With regard to the opposition that we filed in Europe against FibroGen’s European Patent No. 163333, or the ’333 patent, an oral proceeding took place December 8 and 9, 2016. Following the oral proceeding, the European Opposition Division ruled that the patent as granted did not meet the requirements for patentability under the European Patent Convention and, therefore, revoked the patent in its entirety. FibroGen has appealed that decision. Oppositions to the ’155 patent and to the ’153 patent were also filed by Glaxo Group Limited, or Glaxo, and by Bayer Intellectual Property GmbH, Bayer Pharma Aktiengesellschaft, and Bayer Animal Health

GmbH. While, for the reasons set forth in our oppositions, we believe that the ’153 patent and the ’155 patent should be revoked in their entirety, the ultimate outcomes of the oppositions remains uncertain. If the European Patent Office decides not to revoke the ’153 patent or the ’155 patent in their entirety, or only certain claims of those patents, and any surviving claims are determined to encompass our intended use of our lead product candidate, we may not be able to commercialize our lead product candidate in the European Union for its intended use, which could materially adversely affect our business, operating results and financial condition.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

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

Market Price Information

Our common stock began trading on the NASDAQ Global Market on March 20, 2014 under the symbol "AKBA". Prior to that date, there was no established public trading market for our common stock. The following table sets forth, for the periods indicated, the high and low intraday sales prices of our common stock as reported by the NASDAQ Global Market:

	High	Low
2016		
First Quarter	$12.74	$7.02
Second Quarter	$9.99	$7.00
Third Quarter	$9.38	$7.31
Fourth Quarter	$11.07	$7.16

	High	Low
2015		
First Quarter	$13.90	$8.47
Second Quarter	$11.12	$7.27
Third Quarter	$14.20	$5.91
Fourth Quarter	$13.20	$7.91

Holders

At March 1, 2017, there were approximately 27 holders of record of our common stock.

Dividends

We have never declared or paid any cash dividends on our common stock and our ability to pay cash dividends is currently prohibited by the terms of our debt financing arrangements. We currently intend to retain earnings, if any, for use in our business and do not anticipate paying cash dividends on our common stock in the foreseeable future. Payment of future dividends, if any, on our common stock will be at the discretion of our board of directors after taking into account various factors, including our financial condition, operating results, anticipated cash needs, and plans for expansion.

Issuer Purchases of Equity Securities

There were no repurchases of shares of common stock made during the year ended December 31, 2016.

Comparative Stock Performance Graph

The information included under the heading “Comparative Stock Performance Graph” in this Item 5 of Part II of this annual report on Form 10-K shall not be deemed to be “soliciting material” or subject to Regulation 14A or 14C, shall not be deemed “filed” for purposes of Section 18 of the Exchange Act, or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1934, as amended, or the Exchange Act.

Set forth below is a graph comparing the total cumulative returns of Akebia Therapeutics, Inc., the NASDAQ Composite Index and the NASDAQ Biotechnology Index. The graph assumes $100 was invested on March 20, 2014 in our common stock and each of the indices and that all dividends, if any, are reinvested.

Equity Compensation Plan Information

We have two equity compensation plans, which have both been approved by our shareholders: the 2014 Incentive Plan and the 2014 Employee Stock Purchase Plan.

The following table sets forth the number and weighted-average exercise price of ordinary shares to be issued upon exercise of outstanding options and the number of securities remaining available for future issuance under all of our equity compensation plans, at December 31, 2016.

Plan Category	Number of securities to be issued upon exercise of outstanding options, warrants and rights (a)	Weighted-average exercise price of outstanding options, warrants and rights (b)	Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a)) (c)
Equity compensation plans approved by security holders	3,190,538	$ 8.97	1,688,433
Equity compensation plans not approved by security holders	255,000	—	—
Total	3,445,538	$ 8.97	1,688,433

Item 6. Selected Financial Data

The consolidated financial data for the years ended December 31, 2016, 2015 and 2014 and as of December 31, 2016 and 2015 is derived from our audited consolidated financial statements, which are included elsewhere in this Annual Report on Form 10-K. The consolidated financial data for the years ended December 31, 2013 and 2012 and as of December 31, 2014, 2013 and 2012 is derived from our audited consolidated financial statements that are not included elsewhere in this Annual Report on Form 10-K. You should read this data together with our consolidated financial statements and related notes included elsewhere in this Annual Report on Form 10-K under the captions "Consolidated Financial Statements and Supplementary Data" and "Management's Discussion and Analysis of Financial Condition and Results of Operations." Our historical results for any prior period are not necessarily indicative of results to be expected in any future period, and our interim period results are not necessarily indicative of results to be expected for a full year or any other interim period.

	Year Ended December 31,				
	2016	2015	2014	2013	2012
	(in thousands, except share and per share data)				
Consolidated statements of operations data:					
Collaboration revenue	$1,535	$—	$—	$—	$—
Operating expenses:					
Research and development	115,785	43,016	23,263	8,902	5,032
General and administrative	22,210	18,497	14,677	7,031	3,491
Total operating expenses	137,995	61,513	37,940	15,933	8,523
Loss from operations	(136,460)	(61,513)	(37,940)	(15,933)	(8,523)
Other income, net	713	797	906	2,766	327
Net loss	$(135,747)	$(60,716)	$(37,034)	$(13,167)	$(8,196)
Accretion on preferred stock	—	—	(86,899)	(55,886)	(3,323)
Net loss applicable to common shareholders	$(135,747)	$(60,716)	$(123,933)	$(69,053)	$(11,519)
Net loss per share applicable to common stockholders—basic and diluted[1]	$(3.60)	$(2.29)	$(8.04)	$(126.94)	$(27.82)
Weighted-average number of common shares used in net loss per share applicable to common stockholders—basic and diluted	37,716,949	26,469,170	15,406,386	544,002	414,107

(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 share of common stock.

	December 31,				
	2016	2015	2014	2013	2012
	(in thousands)				
Balance Sheet Data:					
Cash and cash equivalents and available for sale securities	$260,343	$138,454	$108,918	$32,556	$1,641
Working capital	182,053	129,149	103,595	29,529	(2,679)
Total assets	300,216	142,940	110,995	34,665	2,244
Redeemable convertible preferred stock	—	—	—	157,827	56,909
Accumulated deficit	(297,136)	(161,389)	(100,673)	(127,072)	(59,588)
Total stockholders' equity (deficit)	68,120	130,998	104,078	(127,072)	(59,588)

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

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and related notes appearing in this annual report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this annual report on Form 10-K, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this annual report on Form 10-K, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Operating Overview

We are a biopharmaceutical company focused on developing and delivering novel therapeutics for patients based on hypoxia-inducible factor, or HIF, biology, and building our pipeline while leveraging our development and commercial expertise in renal disease. HIF is the primary regulator of the production of red blood cells, or RBCs, in the body, as well as other important metabolic functions. Pharmacologic modulation of the HIF pathway may have broad therapeutic applications. Our lead product candidate, vadadustat, is an oral therapy in Phase 3 development, which has the potential to set a new standard of care in the treatment of anemia associated with chronic kidney disease (CKD). Our management team has extensive experience in developing and commercializing drugs for the treatment of renal and metabolic disorders, as well as a deep understanding of HIF biology. This unique combination of HIF and renal expertise is enabling us to advance a pipeline of HIF-based therapies to address serious diseases.

HIF, a pathway involving hundreds of genes, is responsible for orchestrating the body's natural response to lower levels of oxygen, or hypoxia. In response to hypoxia, a coordinated adaptive response occurs resulting in both an increase in red blood cell production, a normal biological process known as erythropoiesis, and enhancement of the delivery of iron to the bone marrow to support erythropoiesis. The significance of the HIF pathway was recognized by the 2016 Albert Lasker Basic Medical Research Award, which honored the three physician-scientists who discovered the HIF pathway and elucidated this primary oxygen sensing mechanism that is essential for survival. HIF protein is constantly being produced under normal oxygen conditions, but is quickly degraded by prolyl hydroxylases, or PH. Under hypoxic conditions, HIF-PH's are inhibited, allowing HIF to stimulate erythropoiesis. These findings have opened up new possibilities for developing therapeutics, such as HIF-PHI, which have the potential to treat many diseases.

Our lead product candidate, vadadustat, a HIF-PH inhibitor in Phase 3 development for the treatment of anemia of CKD. Anemia is a serious medical condition in which blood is deficient in hemoglobin, which is critical for delivering oxygen to organs and tissue. Untreated anemia is associated with chronic fatigue, increased risk of progression of multiple diseases and death. Anemia is common in patients with CKD, cancer, heart failure, inflammatory diseases and other critical illnesses.

More than 30 million people in the United States have CKD, with estimates that over 1.8 million of these patients suffer from anemia. Anemia from CKD is currently treated by injectable recombinant erythropoiesis-stimulating agents, or rESAs, such as EPOGEN® and Aranesp®, as well as with iron supplementation or red blood cell transfusion. Based on the reported revenues of companies that market and sell rESAs, global sales of injectable rESAs were estimated to be between $6.5 and $7.0 billion in 2015. The vast majority of these sales were for the treatment of anemia associated with renal disease.

rESAs deliver supra-physiological levels of exogenous erythropoietin, or EPO, to stimulate production of RBCs. While injectable rESAs may be effective in raising hemoglobin levels, they carry significant potential side effects, and need to be injected under the skin (subcutaneously) or into a vein (intravenously). In particular, injectable rESAs may lead to thrombosis, stroke, myocardial infarction and death. These safety concerns, which became evident starting in

2006, have led to a significant reduction in the use of injectable rESAs. Today, anemia is either not treated or inadequately treated in the majority of non-dialysis dependent (NDD) CKD patients. We believe that novel treatment options that address these concerns are needed and would have significant market potential. Because it mimics the body's natural adaptive response to hypoxia, vadadustat's HIF-PH inhibition may raise hemoglobin levels without causing supra-physiological levels of EPO.

Vadadustat has the potential to set a new standard of care for the treatment of anemia in CKD. Early clinical studies of vadadustat demonstrated that diurnal variation of EPO was maintained resulting in predictable increases in hemoglobin in normal human volunteers and similar results were seen in NDD-CKD. These data led us to the design of our Phase 3 clinical program. The vadadustat Phase 3 program in NDD-CKD patients with anemia, called PRO_2TECT, and in dialysis dependent (DD) CKD patients with anemia, called $INNO_2VATE$, is designed to enroll approximately 5,700 patients evaluating once daily oral dosing of vadadustat against an rESA active comparator, darbepoetin alfa. The enrollment numbers and the completion of the Phase 3 program will be driven by the rate of major adverse cardiovascular events, or MACE. In December 2015 the first patient was dosed in PRO_2TECT, and the first patient was dosed in $INNO_2VATE$ in August 2016. We plan to initiate a Phase 3 study in the second half of 2017 to evaluate three-times weekly dosing of vadadustat in approximately 300 DD-CKD patients receiving hemodialysis using the same active comparator, darbepoetin

alfa. We currently anticipate submitting marketing applications for the treatment of anemia associated with CKD in the United States and Europe in 2019.

If vadadustat is approved by the United States Food and Drug Administration, or FDA, we plan to establish our own commercial organization in the United States while leveraging our collaboration with Otsuka Pharmaceutical Co. Ltd., or Otsuka, and its well-established commercial organization. In Japan and other countries in Asia, we plan to commercialize vadadustat through our collaboration with Mitsubishi Tanabe Pharma Corporation, or MTPC, and intend to seek one or more collaborators to commercialize vadadustat in Europe and other markets.

In addition to vadadustat, we are developing a HIF-based portfolio of product candidates that target serious diseases of high unmet need. Our portfolio includes product candidates developed internally, such as AKB-6899, as well as in-licensed product candidates, such as AKB-5169. AKB-6899 has demonstrated a robust hemoglobin response in early preclinical studies, and we plan to further investigate its potential in multiple preclinical models of anemia and assess next steps based on these data. In February 2017, we signed an agreement with Janssen Pharmaceutica NV, or Janssen, for access to an extensive library of well-characterized HIF pathway compounds with potential applications across multiple therapeutic areas. The lead compound, AKB-5169, is a differentiated preclinical compound in development as an oral treatment for inflammatory bowel disease (IBD) and we intend to complete further preclinical development with the goal of an Investigational New Drug application with the FDA in 2018.

Since our inception in 2007, we have devoted the largest portion of our resources to our development efforts relating to vadadustat, including preparing for and conducting clinical studies of vadadustat, providing general and administrative support for these operations and protecting our intellectual property. We do not have any products approved for sale and have not generated any revenue from product sales. We have funded our operations primarily through equity offerings and strategic collaborations.

We have never been profitable and have incurred net losses in each year since inception. Our net losses were $135.7 million, $60.7 million and $37.0 million for the years ended December 31, 2016, 2015 and 2014, respectively. Substantially all of our net losses resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations.

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

- complete the development of vadadustat for anemia secondary to CKD;
- seek regulatory approvals for our product candidates that successfully complete clinical trials;
- have our product candidates manufactured for clinical trials and for commercial sale;
- establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval;
- initiate and continue preclinical and clinical development of our HIF compounds and product candidates;
- initiate additional preclinical, clinical or other studies for additional indications for vadadustat;
- seek to discover and develop additional product candidates;
- acquire, in-license and develop other commercial products, product candidates and technologies;
- make royalty, milestone or other payments under any future in-license agreements;
- maintain, protect and expand our intellectual property portfolio;
- attract and retain skilled personnel; and
- create additional infrastructure to support our operations as a public company.

We do not expect to generate revenue from product sales unless and until we successfully complete development and obtain regulatory approval for one or more of our product candidates, which we expect will take a number of years and is subject to significant uncertainty. We have no manufacturing facilities, and all of our manufacturing activities

are contracted out to third parties. Additionally, we currently utilize third-party contract research organizations, or CROs, to carry out our clinical development activities, and we do not yet have a sales organization. If we obtain regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. Accordingly, we will seek to fund our operations through public or private equity or debt financings or other sources including geographic partnerships. However, we may be unable to raise additional funds or enter into other arrangements when needed on favorable terms or at all. Our

failure to raise capital or enter into such other arrangements as and when needed would have a negative impact on our financial condition and our ability to develop our products.

On March 6, 2014, we effected a 1.75-for-1 stock split of our outstanding common stock. Our historical share and per share information have been retroactively adjusted to give effect to this stock split. Shares of common stock underlying outstanding stock options and other equity instruments were proportionately increased and the respective exercise prices, if applicable, were proportionately reduced in accordance with the terms of the agreements governing such securities. Shares of common stock reserved for issuance upon the conversion of our Series A Redeemable Convertible Preferred Stock, Series B Redeemable Convertible Preferred Stock and Series C Redeemable Convertible Preferred Stock were proportionately increased, and the respective conversion prices were proportionately reduced.

Through 2016 we have raised approximately $254.1 million of net proceeds from five underwritten public offerings, including $61.0 million of net proceeds raised in January 2016 whereby we sold 7,250,000 shares of common stock at a price of $9.00 per share and $5.7 million of net proceeds whereby we sold 615,293 shares of common in an at-the-market offering, or ATM, pursuant to a Sales Agreement with Cantor Fitzgerald & Co. entered into in May 2016.

Financial Overview

In the quarter ended December 31, 2015, we identified and corrected an error in the historical classification of certain operating costs between research and development and general and administrative expenses. We concluded the effect of this classification error was not material to our consolidated financial statements for any prior period. The classification correction had no effect on our current or historical total operating expenses or net loss.

Revenue

To date, we have not generated any revenue from the sales of products. Our revenues have been derived from collaboration agreements.

Revenue recognition for our MTPC collaboration will commence when all criteria as required under ASC 605 have been satisfied, which the Company expects will be in the second half of 2017. Therefore, collaboration revenue in 2016 is generated exclusively from our collaboration arrangement with Otsuka. The terms of this arrangement contain multiple deliverables, which include at inception: (i) license under certain of our intellectual property to develop, perform medical affairs activities with respect to and conduct non-promotional and commercialization activities related to vadadustat (the License Deliverable), (ii) development services to be performed pursuant to the current global development plan (the R&D Services Deliverable), (iii) rights to future intellectual property and (iv) joint committee services. We have identified three units of accounting in connection with our obligations under the collaboration agreement with Otsuka as follows: (i) License Unit of Accounting, which combines the License Deliverable and the R&D Services Deliverable (ii) Rights to future intellectual property Unit of Accounting and (iii) Joint committee services Unit of Accounting. We recognize arrangement consideration allocated to each unit of accounting when all of the revenue recognition criteria in Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, Topic 605, Revenue Recognition, or ASC 605, are satisfied for that particular unit of accounting.

The Company will recognize revenue related to amounts allocated to the License Unit of Accounting on a proportional performance basis as the underlying services are performed.

Our ability to generate product revenue and become profitable depends upon our ability to successfully develop and 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 product candidates and begin to commercialize any approved products. Because of the numerous risks and uncertainties associated with product development, we are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability. Even if we are able to generate revenue from the sale of our products, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce our operations.

For the foreseeable future, we expect substantially all of our revenue will be generated from our collaborations with Otsuka and MTPC and any other collaborations we may enter into.

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for the development of our product candidates, which include:

- employee-related expenses, including salaries, benefits, recruiting fees, travel and stock-based compensation expense;
- expenses incurred under agreements with the CROs and investigative sites that conduct our clinical studies;
- the cost of acquiring, developing and manufacturing clinical study materials;
    - facilities, depreciation and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance and other supplies; and
- costs associated with preclinical and clinical activities.

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 studies of our product candidates or if, when, or to what extent we will generate revenue from the commercialization and sale of any of our product candidates that obtain regulatory approval. We may never succeed in achieving regulatory approval for any of our product candidates.

The duration, costs and timing of clinical studies and development of our product candidates will depend on a variety of factors, including:

- the results of our meetings with the FDA and the EMA and other regulatory authorities and the consequential effect on our study design, study size and resulting operating costs;
- the size, rate of progress, results and costs of completing our global Phase 3 development of vadadustat;
- difficulties or delays in enrolling patients in our clinical trials;
- assuming favorable Phase 3 clinical results, the timing of, and the costs involved in, obtaining regulatory approvals for vadadustat in dialysis and non-dialysis indications, including to fund the preparation and filing of regulatory submissions for vadadustat with the FDA, the EMA and other regulatory authorities, and whether we will seek regulatory approval for both indications simultaneously;
- the cost, timing and outcome of our efforts to obtain marketing approval for vadadustat in the United States, Europe and in other jurisdictions;
- the scope, progress, results and costs of additional preclinical, clinical, or other studies for additional indications for vadadustat, as well as any studies of AKB-6899, AKB-5169 and other product candidates that we may develop or acquire;
- the timing of, and the costs involved in, obtaining regulatory approvals for AKB-6899, AKB-5169 and other product candidates that we may develop or acquire, if clinical studies are successful;
- the cost of having our product candidates manufactured for clinical trials;
- the cost and timing of future commercialization activities for our products, if any of our product candidates are approved for marketing, including product manufacturing, marketing, sales and distribution costs;
- our ability to establish and maintain strategic collaborations, licensing or other arrangements and the financial terms of such agreements; and
- unanticipated changes to laws or regulations applicable to our clinical trials.

A change in the outcome of any of these variables with respect to the development of a product candidate could mean a significant change in the costs and timing associated with the development of that product candidate. For example, if the FDA, EMA or another regulatory authority were to require us to conduct clinical studies in addition to or different from those that we currently anticipate, or if we experience significant delays in enrollment in any of our clinical

studies, we could be required to expend significant additional financial resources and time on the completion of clinical development.

From inception through December 31, 2016, we have incurred $231.9 million in research and development expenses. We plan to increase our research and development expenditures for the foreseeable future as we continue the development of vadadustat and our other product candidates. Our current and/or planned research and development activities include the following:

- global development of vadadustat, including the PRO2TECT and INNO2VATE clinical programs;
- research and development of compounds in our HIF portfolio, including product candidates such as AKB-6899 and AKB-5169; and
- diversify our pipeline in kidney disease and other HIF-modulated diseases.

Our direct research and development expenses consist principally of external costs, such as fees paid to clinical trial sites, consultants, central laboratories and CROs in connection with our clinical studies, and costs related to acquiring and manufacturing clinical study materials.

We currently have two programs to which our research and development costs are attributable. Historically, we have not accumulated and tracked our research and development costs or our personnel and personnel-related costs on a program-by-program basis. Our employee and infrastructure resources, and many of our costs, were directed broadly to applicable research endeavors. As a result, we are unable to specify precisely the historical costs incurred for each of our programs on a program-by-program basis.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and related costs for personnel, including stock-based compensation and travel expenses. Other general and administrative expenses include facility-related costs, fees for directors, accounting and legal services fees, recruiting fees and expenses associated with obtaining and maintaining patents.

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 product candidates. We also anticipate increased expenses related to finance, legal, regulatory and tax-related services associated with maintaining compliance with exchange listing and SEC requirements, and our other costs associated with being a public company. Additionally, we anticipate an increase in payroll and related expenses if and when we prepare for commercial operations, especially in sales and marketing.

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 prepaid and accrued research and development 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

We recognize revenue in accordance with Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, Topic 605, Revenue Recognition, or ASC 605. Accordingly, revenue is recognized for each unit of accounting when all of the following criteria are met:

- persuasive evidence of an arrangement exists;
- delivery has occurred or services have been rendered;
- the seller's price to the buyer is fixed or determinable; and
- collectability is reasonably assured.

Amounts received prior to satisfying the revenue recognition criteria are recorded as deferred revenue in our consolidated balance sheets.

Multiple Element Arrangements

Determination of Accounting Units

We analyze multiple element arrangements based on the guidance in ASC Topic 605 25, Revenue Recognition—Multiple Element Arrangements, or ASC 605 25. Pursuant to the guidance in ASC 605 25, we evaluate multiple element arrangements to determine (1) the deliverables included in the arrangement and (2) whether the individual deliverables represent separate units of accounting or whether they must be accounted for as a combined unit of accounting. This evaluation involves subjective determinations and requires management to make judgments about the individual deliverables and whether such deliverables are separate from other aspects of the contractual relationship. Deliverables are considered separate units of accounting provided that: (i) the delivered item(s) has value to the customer on a standalone basis and (ii) if the arrangement includes a general right of return relative to the delivered item(s), delivery or performance of the undelivered item(s) is considered probable and substantially within our control. In assessing whether an item under a collaboration has standalone value, we consider factors such as the research, manufacturing, and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. We also consider whether our collaboration partner can use the other deliverable(s) for their intended purpose without the receipt of the remaining element(s), whether the value of the deliverable is dependent on the undelivered item(s), and whether there are other vendors that can provide the undelivered element(s).

Options under a collaboration are considered substantive if, at the inception of the arrangement, we are at risk as to whether the collaboration partner will choose to exercise the option. Factors that we consider in evaluating whether an option is substantive include the cost to exercise the option, the overall objective of the arrangement, the benefit the collaboration partner might obtain from the arrangement without exercising the option, and the likelihood the option will be exercised. When an option is considered substantive, we would not consider the option or item underlying the option to be a deliverable at the inception of the arrangement and the associated option fees are not included in allocable consideration, assuming the option is not priced at a significant and incremental discount. Conversely, when an option is not considered substantive, we would consider the option, including other deliverables contingent upon the exercise of the option, to be a deliverable at the inception of the arrangement and a corresponding amount would be included in allocable arrangement consideration. In addition, if the price of the option includes a significant incremental discount, the discount would be included as a deliverable at the inception of the arrangement.

Allocation of Arrangement Consideration

Arrangement consideration that is fixed or determinable is allocated among the separate units of accounting using the relative selling price method. The applicable revenue recognition criteria in ASC 605 are applied to each of the separate units of accounting in determining the appropriate period and pattern of recognition. We determine the selling price of a unit of accounting following the hierarchy of evidence prescribed by ASC 605 25. Accordingly, we determine the estimated selling price for units of accounting within each arrangement using vendor specific objective evidence, or VSOE, of selling price, if available, third party evidence, or TPE, of selling price if VSOE is not available, or best estimate of selling price, or BESP, if neither VSOE or TPE is available. We have only used BESP to estimate selling price, since we have not had VSOE or TPE of selling price for any units of accounting to date. Determining BESP for a unit of accounting requires significant judgment. In developing the BESP for a unit of accounting, we consider applicable market conditions and relevant entity specific factors, including factors that were contemplated in negotiating the applicable agreement and estimated costs. We validate BESP for units of accounting by evaluating whether changes in the key assumptions used by us to determine the BESP will have a significant effect

on the allocation of arrangement consideration between multiple units of accounting.

Pattern of Recognition

We recognize the arrangement's consideration allocated to each unit of accounting when all of the revenue recognition criteria in ASC 605 are satisfied for that particular unit of accounting. We recognize revenue associated with licenses, license options, or the discount related to a license option upon (i) delivery of the license or (ii) the earlier of exercise or expiration of the license option, if the underlying license has standalone value from the other deliverables to be provided after delivering that license. If the license does not have standalone value, the amounts allocated to the license are combined with the related undelivered items as a single unit of accounting.

We recognize the amounts associated with collaboration research and development services, joint research committees, or other services ratably over the associated period of performance. If there is no discernible pattern of performance or objectively measurable performance measures do not exist, then we recognize revenue under the arrangement on a straight line basis over the

period that we are expected to complete our performance obligations. Conversely, if the pattern of performance in which the service is provided to the collaboration partner can be determined and objectively measureable performance exists, then we recognize revenue under the arrangement using the proportional performance method. Revenue to be recognized is limited to the lesser of the cumulative amount of payments received or the cumulative revenue earned determined using the straight line method or proportional performance, as applicable, as of the period end date.

Recognition of Milestones and Royalties

At the inception of an arrangement that includes milestone payments, we evaluate whether each milestone is substantive and at risk to both parties on the basis of the contingent nature of the milestone. This evaluation includes an assessment of whether: (1) the consideration is commensurate with either our performance to achieve the milestone or the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from our performance to achieve the milestone, (2) the consideration relates solely to past performance, and (3) the consideration is reasonably relative to all of the deliverables and payment terms within the arrangement. We evaluate factors such as clinical, regulatory, commercial, and other risks that must be overcome to achieve the respective milestones and the level of effort and investment required to achieve the respective milestones in making this assessment. There is considerable judgment involved in determining whether a milestone satisfies all of the criteria required to conclude that a milestone is substantive. In accordance with ASC Topic 605 28, Revenue Recognition—Milestone Method, or ASC 605 28, a clinical or regulatory milestone that is considered substantive will be recognized as revenue in its entirety upon successful accomplishment of the milestone, assuming all other revenue recognition criteria are met. Milestones that are not considered substantive would be recognized as revenue over the remaining period of performance, assuming all other revenue recognition criteria are met. Revenue from a commercial milestone payment will be accounted for as royalties and recorded as revenue upon achievement of the milestone, assuming all other revenue recognition criteria are met.

We will recognize royalty revenue in the period of sale of the related product(s), based on the underlying contract terms, provided that the reported sales are reliably measurable, we have no remaining performance obligations, and assuming all other revenue recognition criteria are met.

Prepaid and Accrued Research and Development Expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate our prepaid and accrued research and development expenses. This process involves reviewing open 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. The majority of our service providers invoice us monthly in arrears for services performed. We make estimates of our prepaid and accrued research and development expenses as of each balance sheet date in our consolidated financial statements based on facts and circumstances known to us at that time. We confirm the accuracy of our estimates with the service providers and make adjustments if necessary. Examples of estimated prepaid and accrued research and development expenses include expenses for:

- CROs in connection with clinical studies;
- 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 materials.

We base our expenses related to clinical studies on our estimates of the services received and efforts expended pursuant to contracts with multiple CROs that conduct and manage clinical studies on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. The scope of services under contracts for research and development activities can be modified and some of the

agreements may be cancelled by either party upon written notice. 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 clinical expense. Payments under some of these contracts depend on factors such as the successful enrollment of subjects and the completion of clinical study milestones. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid accordingly.

Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed we may report amounts that are too high or too low in any particular period. To date, there have been no material differences between our estimates and the amount actually incurred.

Stock-Based Compensation

Stock-Based Awards

We issue stock-based awards to employees and non-employees, generally in the form of stock options, restricted stock, RSUs and shares of common stock. We account for our stock-based compensation awards in accordance with Financial Accounting Standards Board, (FASB) ASC Topic 718, Compensation—Stock Compensation, or ASC 718. ASC 718 requires all stock-based payments to employees, including grants of employee stock options and restricted stock and modifications to existing stock awards, to be recognized in the statements of operations and comprehensive loss based on their fair values. We account for stock-based awards to non-employees in accordance with ASC Topic 505-50, Equity-Based-Payments to Non-Employees, or ASC 505-50, which requires the fair value of the award to be re-measured at fair value until a performance commitment is reached or counterparty performance is complete. Described below is the methodology we have utilized in measuring stock-based compensation expense. Stock option, common stock and restricted stock values are determined based on the quoted market price of our comparable public companies.

We estimate the fair value of our stock-based awards of options to purchase shares of common stock to employees and non-employees using the Black-Scholes option pricing model, which requires the input of highly subjective assumptions, including (a) the expected stock price volatility, (b) the calculation of the expected term of the award, (c) the risk-free interest rate and (d) expected dividends. Due to the lack of company-specific historical and implied volatility data for trading our stock in the public market, we have based our estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. The historical volatility is calculated based on a period of time commensurate with the expected term assumption. The computation of expected volatility is based on the historical volatility of a representative group of companies with similar characteristics to our company, including stage of product development and life science industry focus. We are a company in the product development stage with no revenue and the representative group of companies has certain similar characteristics. We believe the group selected has sufficient similar economic and industry characteristics, and includes companies that are most representative of our company. We use the simplified method as prescribed by the SEC Staff Accounting Bulletin No. 107, Share-Based Payment, to calculate the expected term for options granted to employees as we do not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. The expected term is applied to the stock option grant group as a whole, as we do not expect substantially different exercise or post-vesting termination behavior among our employee population. For options granted to non-employees, we utilize the contractual term of the arrangement as the basis for the expected term assumption. The risk-free interest rate is based on a treasury instrument whose term is consistent with the expected life of the stock options. The expected dividend yield is assumed to be zero as we have never paid dividends and have no current plans to pay any dividends on our common stock, similar to our peer group. We estimate grant date fair value of restricted stock awards with corresponding promissory notes using the Black-Scholes option pricing model. The grant date fair value of restricted stock awards and awards of common stock has been based on the estimated value of our common stock at the date of grant.

Our stock-based awards are subject to service-based vesting conditions. Compensation expense related to awards to employees with service-based vesting conditions is recognized on a straight-line basis based on the grant date fair value over the associated service period of the award, which is generally the vesting term. Consistent with the guidance in ASC 505-50, compensation expense related to awards to non-employees with service-based vesting conditions is recognized on a straight-line basis based on the then-current fair value at each financial reporting date prior to the measurement date over the associated service period of the award, which is generally the vesting term.

We are also required to estimate forfeitures at the time of grant, and revise those estimates in subsequent periods if actual forfeitures differ from our estimates. We use historical data to estimate pre-vesting forfeitures and record

stock-based compensation expense only for those awards that are expected to vest. To the extent that actual forfeitures differ from our estimates, the difference is recorded as a cumulative adjustment in the period the estimates were revised. Stock-based compensation expense recognized in the consolidated financial statements is based on awards that are ultimately expected to vest.

Stock-based compensation expense totaled approximately $5.8 million, $4.7 million and $6.0 million for the years ended December 31, 2016, 2015 and 2014, respectively.

We expect the impact of our stock-based compensation expense for stock options and restricted stock granted to employees and non-employees to grow in future periods due to the potential increases in the fair value of our common stock and the increase in the number of grants as a result of an increase in headcount.

Emerging Growth Company Status

The JOBS Act permits an “emerging growth company” to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies. We chose to “opt out” of this provision and, as a result, we will comply

with new or revised accounting standards as required when they are adopted. This decision to opt out of the extended transition period under the JOBS Act is irrevocable.

Results of Operations

Comparison of the Years Ended December 31, 2016 and 2015

	Year ended December 31,		Increase (Decrease)
	2016	2015	
	(In Thousands)		
Collaboration revenue	$ 1,535	$—	$ 1,535
Operating expenses:			
Research and development	115,785	43,016	72,769
General and administrative	22,210	18,497	3,713
Total operating expenses	137,995	61,513	76,482
Loss from operations	(136,460)	(61,513)	(74,947)
Other income, net	713	797	(84)
Net loss	$(135,747)	$(60,716)	$ (75,031)

Collaboration Revenue. Collaboration revenue was $1.5 million for the year ended December 31, 2016 under our agreement with Otsuka.

Research and Development Expenses. Research and development expenses were $115.8 million for the year ended December 31, 2016, compared to $43.0 million for the year ended December 31, 2015. The increase of $72.8 million was primarily due to the following:

	(in millions)
Vadadustat development	$ 65.5
Manufacture of drug substance	3.1
Regulatory and other clinical and non-clinical activities	(2.7)
Total increase related to the continued development of vadadustat	65.9
Headcount, consulting and facilities	6.5
Other	0.4
Total net increase	$ 72.8

The increase in the costs related to the development of vadadustat is primarily attributable to external costs related to the PRO$_2$TECT and INNO$_2$VATE Phase 3 program. The increase in headcount, consulting and facility related costs is

primarily due to additional headcount and consulting costs to support the Phase 3 programs as well as rent associated with our leasing of additional office and lab space to support our additional headcount. We expect our research and development expenses to increase in future periods in support of the Phase 3 programs and other studies and our pipeline development.

General and Administrative Expenses. General and administrative expenses were $22.2 million for the year ended December 31, 2016, compared to $18.5 million for the year ended December 31, 2015. The increase of $3.7 million was primarily due to an increase in costs to support our Phase 3 program, including: $3.1 million of headcount and compensation-related costs and $0.7 million in facility-related costs. We expect our general and administrative expenses to increase in future periods in support of the Phase 3 programs.

Other Income, Net. Other income, net, was $0.7 million for the year ended December 31, 2016, compared to $0.8 million for the year ended December 31, 2015. Other income, net for the year ended December 31, 2016, is primarily comprised of interest income partially offset by expenses related to the write-off of capitalized software. Other income, net for the year ended December 31, 2015 is primarily related to reimbursements under a services agreement for employee-related costs of approximately $0.3 million and interest income of approximately $0.5 million. The decrease in reimbursements related to the services agreement for employee-related costs is principally the result of our employees no longer providing services under this agreement.

Comparison of the Years Ended December 31, 2015 and 2014

	Year ended December 31,		Increase (Decrease)
	2015	2014	
	(In Thousands)		
Operating expenses:			
Research and development	$43,016	$23,263	$ 19,753
General and administrative	18,497	14,677	3,820
Total operating expenses	61,513	37,940	23,573
Loss from operations	(61,513)	(37,940)	23,573
Other income, net	797	906	(109)
Net loss	$(60,716)	$(37,034)	$ 23,682

Research and Development Expenses. Research and development expenses were $43.0 million for the year ended December 31, 2015, compared to $23.3 million for the year ended December 31, 2014. The increase of $19.7 million was primarily due to the following:

	(in millions)
Preparation for the PRO2TECT Phase 3 program	$ 14.2
Other clinical and non-clinical	2.7
Regulatory activities	1.2
Completion of Phase 2b study in non-dialysis patients with anemia related to CKD	(4.8)
Ongoing Phase 2 study for the treatment of anemia in patients undergoing dialysis	(0.8)
Total increase related to the continued development of vadadustat	12.5
Headcount and consulting	4.6
Drug development for AKB-6899	2.2
Other	1.2
Stock compensation	(0.7)
Total net increase	$ 19.8

General and Administrative Expenses. General and administrative expenses were $18.5 million for the year ended December 31, 2015, compared to $14.7 million for the year ended December 31, 2014. The increase of $3.8 million was primarily due to the following expense increases: $1.2 million of wage and personnel-related costs due to additional headcount, $1.4 million in commercial planning costs, $0.7 million in legal costs and $0.7 million related to facilities.

Other Income, Net. Other income, net, was $0.8 million for the year ended December 31, 2015, compared to $0.9 million for the year ended December 31, 2014. Other income, net for the year ended December 31, 2015, is primarily related to reimbursements under a services agreement for employee-related costs of approximately $0.3 million and interest income of approximately $0.5 million. Other income, net for the year ended December 31, 2014 is primarily related to reimbursements under a services agreement for employee-related costs of approximately $0.7 million and interest income of approximately $0.2 million. The decrease in reimbursements related to the services agreement for employee-related costs is principally the result of reduced time spent by our employees on the services agreement related activities.

Liquidity and Capital Resources

We have incurred losses and cumulative negative cash flows from operations since our inception in February 2007, and as of December 31, 2016, we had an accumulated deficit of $297.1 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 equity offerings, debt financings, other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements.

We have funded our operations principally through equity offerings and payments received from our collaboration partners. As of December 31, 2016, we had cash and cash equivalents and available for sale securities of approximately $260.3 million. Cash in excess of immediate requirements is invested in accordance with our investment policy, primarily with a view to liquidity and capital preservation. Accordingly, available for sale securities, consisting principally of corporate and government debt securities stated at fair value, are also available as a source of liquidity.

Cash Flows

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

	Year ended December 31,		
	2016	2015	2014
	(In Thousands)		
Net cash provided by (used in):			
Operating activities	$57,906	$(52,407)	$(27,483)
Investing activities	12,705	(13,688)	(65,352)
Financing activities	66,946	83,093	104,400
Net increase in cash and cash equivalents	$137,557	$16,998	$11,565

Operating Activities. During the year ended December 31, 2016, our operating activities provided net cash of $57.9 million and during the years ended December 31, 2015 and 2014, our operating activities used net cash of $52.4 million and $27.5 million, respectively. The net cash provided by operating activities in 2016 primarily resulted from our net loss, offset by an increase in our working capital accounts, including an increase in deferred revenue of $197.0 million related to upfront or unbilled payments from MTPC and Otsuka and an increase in accrued expense of $20.2 million. The increase in net cash used in operations for the year ended December 31, 2015 as compared to the year ended December 31, 2014 was due primarily to higher operating expenses during the year ended December 31, 2015 of $61.5 million as compared to $37.9 million for the year ended December 31, 2014 adjusted for non-cash items, including stock-based compensation of $4.7 million in 2015.

Investing Activities. During the year ended December 31, 2016, our investing activities provided net cash of $12.7 million which was comprised primarily of proceeds from the maturities of available for sale securities, offset by purchases of available for sale securities and purchases of equipment. During the years ended December 31, 2015 and 2014, our investing activities used net cash of $13.7 million and $65.4 million, respectively. Net cash used in investing activities for the years ended December 31, 2015 and 2014 was comprised primarily of purchases of available for sale securities and purchases of equipment, offset by proceeds from the maturities of available for sale securities.

Financing Activities. During the years ended December 31, 2016, 2015 and 2014 our net cash provided by financing activities was $66.9 million, $83.1 million and $104.4 million, respectively. Net cash provided by financing activities

for the year ended December 31, 2016 and 2015 consisted primarily of net proceeds from the issuance of common stock from our follow-on public offerings and ATM offerings. Net cash provided by financing activities for the year ended December 31, 2014 consisted primarily of net proceeds from the issuance of common stock in connection with our initial public offering.

Operating Capital Requirements

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

We ended 2016 with cash, cash equivalents and available for sale securities of $260.3 million and we expect these existing resources together with amounts expected to be received from Otsuka, and MTPC, to fund our current operating plan into mid-2018. However,

we currently estimate we will need additional funds to complete our Phase 3 development of vadadustat, including both the PRO2TECT and INNO2VATE clinical programs. We will need to raise additional funds sooner to pursue development activities related to additional product candidates. If and until we can generate a sufficient amount of revenue from our products, we expect to finance future cash needs through public or private equity, debt offerings, or strategic transactions. We have based these estimates on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. We intend to secure a geographic collaboration for the development and commercialization of vadadustat in Europe and potentially other regions outside of the United States with a goal of providing funds sufficient to enable us to complete our Phase 3 development of vadadustat, including both the PRO_2TECT and $INNO_2$VATE clinical programs. However, our development milestones may not be achieved, we may not receive the anticipated funding from our collaboration partners, we may not be able to secure another collaboration for the development and commercialization of vadadustat and we may not secure other sources of financing to complete our Phase 3 development of vadadustat.

We will require additional capital for the further development of our existing product candidates and will need to raise additional funds sooner to pursue development activities related to additional product candidates. If and until we can generate a sufficient amount of revenue from our products, we expect to finance future cash needs through public or private equity, debt offerings, or strategic transactions. Additional funds may not be available to us on acceptable terms or 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 product candidates. If we raise additional funds through the issuance of additional debt or equity securities, it could result in dilution to our existing stockholders or increased fixed payment obligations, and any such securities may have rights senior to those of our common stock. If we incur indebtedness, we could become subject to covenants that would restrict our operations and potentially impair our competitiveness, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. 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 be substantially different than actual results, 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, those described under Part II, Item 1A Risk Factors of this Annual Report on Form 10-K.

If we cannot expand our operations or otherwise capitalize on our business opportunities because we lack sufficient capital, our business, financial condition and results of operations could be materially adversely affected.

Contractual Obligations and Commitments

We lease approximately 45,362 square feet of office and lab space in Cambridge, Massachusetts under a lease which was most recently amended in July 2016, collectively, the Lease. Total monthly lease payments for base rent are approximately $242,000 per month which is subject to annual rent escalations. In addition to such annual rent escalations, base rent payments for a portion of said premises are scheduled to commence on or about January 1, 2017 in the monthly amount of approximately $22,000. Landlord contributions included in the Lease from the landlord totaled $2,169,920, including $256,765 in leasehold improvements not yet utilized. The landlord contributions are being accounted for as a deferred lease incentive and reduction in monthly rent expense over the term of the Lease. The term of the Lease with respect to the office space expires on September 11, 2026, with one five year extension option available. The term of the Lease for the lab space is five years, with an extension option for one additional period of two years. The total security deposit in connection with the Lease of $1,280,857 is included in other assets in

our consolidated balance sheets as of December 31, 2016 and December 31, 2015.

We recognize rent expense for the space which we currently occupy and record a deferred lease obligation representing the cumulative difference between actual facility lease payments and lease expense recognized ratably over the lease period, which is included in our condensed consolidated balance sheets as of December 31, 2016 and December 31, 2015. We will begin recognizing rent expense for the lab space and the remaining office space subsequent to taking possession of the space.

Under the Lease, the Company took possession of the remaining 3,384 square feet of office space on January 1, 2017, and subleased this space on that date (the Sublease) as it did not intend to use the space for its operations. The term of the Sublease is two years and the monthly rent to be received by the Company is approximately $22,000. Under the Sublease, the Company’s operating lease obligations through 2018 are partially offset by future Sublease payments to it of approximately $0.5 million. The total security deposit in connection with the Sublease of $21,432 which is due within 30 days from the execution of the Sublease, is included in other current assets and other liabilities in the Company’s condensed consolidated balance sheets.

We lease office equipment under three year capital leases with payments commencing in February 2014, April 2015 and February 2016, respectively. The capital lease amounts are included in accrued expenses and other liabilities.

At December 31, 2016, our future minimum payments required under these leases are as follows:

Payments due by period (in thousands)	Total	Less than 1 year	1-3 years	3-5 years	More than 5 years
Capital Lease Obligations	$14	$9	$5	—	—
Operating Lease Obligations	32,357	3,545	10,635	9,755	8,422
Total	$32,371	$3,554	$10,640	$9,755	$8,422

(1) Our commitments for operating leases relate to our lease of office and laboratory space in Cambridge, Massachusetts. In December 2016, we entered into an arrangement, with the landlord's consent, to sublease a portion of our Cambridge, Massachusetts corporate headquarters. The future minimum lease payments included in this table do not reflect approximately $0.5 million of sublease rental income that we are entitled to receive through 2018.

Under our agreement with a subsidiary of Quintiles IMS Holdings, Inc., or Quintiles, to provide services for the PRO_2TECT and $INNO_2$VATE programs, the total remaining contract costs as of December 31, 2016 were approximately $406.4 million. The estimated period of performance for the committed work with Quintiles is through the fourth quarter of 2019. We contract with various other organizations to conduct research and development activities with remaining contract costs to us of approximately $24.9 million as of December 31, 2016. The scope of the services under contracts for research and development activities can be modified and the contracts cancelled by the Company upon written notice. In some instances, the contracts may be cancelled by the third party upon written notice.

Off-Balance Sheet Arrangements

As of December 31, 2016 we did not have any off-balance sheet arrangements as defined in the rules and regulations of the SEC.

Item 7A. Quantitative and Qualitative Disclosures about Market Risk

We are exposed to market risk related to changes in interest rates. As of December 31, 2016 and 2015, we had cash and cash equivalents and available for sale securities of $260.3 million and $138.5 million, respectively, primarily money market mutual funds consisting of U.S. government debt securities, certificates of deposit and corporate debt securities. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments are in short-term securities. Our investments are subject to interest rate risk and will fall in value if market interest rates increase. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our portfolio.

Item 8. Financial Statements and Supplementary Data
Akebia Therapeutics, Inc.

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Report of Independent Registered Public Accounting Firm

The Board of Directors and Shareholders of

Akebia Therapeutics, Inc.

We have audited the accompanying consolidated balance sheets of Akebia Therapeutics, Inc. (the "Company") as of December 31, 2016 and 2015, and the related consolidated statements of operations and comprehensive loss, redeemable convertible preferred stock and stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2016. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company's internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Akebia Therapeutics, Inc. at December 31, 2016 and 2015, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2016, in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP

Boston, Massachusetts

March 6, 2017

AKEBIA THERAPEUTICS, INC.

Consolidated Balance Sheets

(in thousands, except share and per share data)

	December 31, 2016	December 31, 2015
Assets		
Current assets:		
Cash and cash equivalents	$ 187,335	$ 49,778
Available for sale securities	73,008	88,676
Unbilled receivable	33,823	—
Prepaid expenses and other current assets	2,155	2,563
Total current assets	296,321	141,017
Property and equipment, net	2,612	540
Deferred offering costs	—	102
Other assets	1,283	1,281
Total assets	$ 300,216	$ 142,940
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 2,039	$ 2,313
Accrued expenses	30,261	9,555
Short-term deferred revenue	81,968	—
Total current liabilities	114,268	11,868
Deferred rent	2,480	69
Deferred revenue, net of current portion	115,321	—
Other non-current liabilities	27	5
Total liabilities	232,096	11,942
Commitments and contingencies (Note 8)		
Stockholders' equity:		
Preferred stock $0.00001 par value, 25,000,000 shares authorized at December 31, 2016 and 31, 2015; 0 shares issued and outstanding at December 31, 2016 and 2015	—	—
Common stock: $0.00001 par value; 175,000,000 shares authorized at December 31, 2016 and 2015; 38,615,709 and 30,662,218 shares issued and outstanding at December 31, 2016 and 2015, respectively	—	—
Additional paid-in capital	365,298	292,783
Treasury stock, at cost, 0 shares at December 31, 2016 and 8,643 shares at December 31, 2015	—	(162)
Accumulated other comprehensive income (loss)	(42)	(234)
Accumulated deficit	(297,136)	(161,389)
Total stockholders' equity	68,120	130,998

Total liabilities and stockholders' equity	$ 300,216	$ 142,940

See accompanying notes to consolidated financial statements.

AKEBIA THERAPEUTICS, INC.

Consolidated Statements of Operations and Comprehensive Loss

(in thousands, except share and per share data)

	Year Ended December 31,		
	2016	2015	2014
Collaboration revenue	1,535	$—	$—
Operating expenses:			
Research and development	115,785	43,016	23,263
General and administrative	22,210	18,497	14,677
Total operating expenses	137,995	61,513	37,940
Operating loss	(136,460)	(61,513)	(37,940)
Other income (expense):			
Interest income	901	510	206
Other income	(188)	287	700
Net loss	$(135,747)	$(60,716)	$(37,034)
Reconciliation of net loss to net loss applicable to common shareholders:			
Net loss	(135,747)	(60,716)	(37,034)
Accretion on preferred stock	—	—	(86,899)
Net loss applicable to common stockholders - basic and diluted	$(135,747)	$(60,716)	$(123,933)
Net loss per share applicable to common stockholders - basic and diluted	$(3.60)	$(2.29)	$(8.04)
Weighted-average number of common shares used in net loss per share applicable to common stockholders—basic and diluted	37,716,949	26,469,170	15,406,386
Comprehensive loss:			
Net loss	$(135,747)	$(60,716)	$(37,034)
Other comprehensive income (loss) - unrealized gain (loss) on securities	(42)	(234)	(56)
Comprehensive loss	$(135,789)	$(60,950)	$(37,090)

See accompanying notes to consolidated financial statements.

Akebia Therapeutics, Inc.

Consolidated Statements of Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)

(in thousands, except share and per share data)

	Redeemable Convertible Preferred Stock Series A, Series B and Series C		Stockholders' Equity (Deficit)						
	Redeemable Convertible Preferred Stock		Common Stock $0.00001 Par Value		Additional Paid-In Capital	Treasury Stock	Unrealized Gain/Loss	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Number of Shares	Amount	Number of Shares						
Balance at December 31, 2013	5,324,948	157,827	1,383,345	—	—	—	—	(127,072)	(127,072)
Issuance of common stock	—	—	6,762,000	—	114,954	—	—	—	114,954
Issuance of restricted common stock	—	—	56,000	—	—	—	—	—	—
Forfeitures of restricted common stock	—	—	(53,835)	—	—	—	—	—	—
Receipt of payment on promissory notes issued in exchange for shares of common stock	—	—	—	—	237	—	—	—	237
Exercise of options	—	—	116,394	—	89	—	—	—	89
Accretion of preferred stock to	—	86,900	—	—	(85,663)	—	—	(1,237)	(86,900)

redemption value									
Conversion of preferred stock	(5,324,948)	(244,727)	12,115,183	—	180,057	—	—	64,670	244,727
Share-based compensation expense	—	—	—	—	6,010	—	—	—	6,010
Deferred offering costs- IPO	—	—	—	—	(10,715)	—	—	—	(10,715)
Unrealized gain/loss	—	—	—	—	—	—	(56)	—	(56)
Treasury shares purchased, not retired (2,553)	—	—	(2,553)	—	—	(94)	—	—	(94)
Treasury shares purchased, retired (5,910)	—	—	(5,910)	—	—	(68)	—	—	(68)
Net income (loss)	—	—	—	—	—	—	—	(37,034)	(37,034)
Balance at December 31, 2014	—	—	20,370,624	—	204,969	(162)	(56)	(100,673)	104,078
Issuance of common stock, net of issuance costs	—	—	10,083,070	—	82,750	—	—	—	82,750
Proceeds from sale of stock under employee stock purchase plan	—	—	25,903	—	220	—	—	—	220
Forfeitures of restricted common stock	—	—	(36,053)	—	—	—	—	—	—
Exercise of options	—	—	218,674	—	130	—	—	—	130
Share-based compensation expense	—	—	—	—	4,714	—	—	—	4,714
Unrealized gain/loss	—	—	—	—	—	—	(178)	—	(178)
Net income (loss)	—	—	—	—	—	—	—	(60,716)	(60,716)
Balance at December 31, 2015	—	—	30,662,218	—	292,783	(162)	(234)	(161,389)	130,998
Issuance of common stock, net of	—	—	7,865,293	—	66,623	—	—	—	66,623

issuance costs									
Proceeds from sale of stock under employee stock purchase plan	—	—	16,629	—	105	—	—	—	105
Forfeitures of restricted common stock	—	—	(15,056)	—	—	—	—	—	—
Exercise of options	—	—	86,625	—	124	—	—	—	124
Share-based compensation expense	—	—	—	—	5,825	—	—	—	5,825
Unrealized gain/loss	—	—	—	—	—	—	192	—	192
Treasury shares retired (8,643)			—	—	(162)	162	—	—	—
Net income (loss)	—	—	—	—	—	—	—	(135,747)	(135,747)
Balance at December 31, 2016	—	—	38,615,709	—	365,298	0	(42)	(297,136)	68,120

See accompanying notes to consolidated financial statements.

AKEBIA THERAPEUTICS, INC.

Consolidated Statements of Cash Flows

(in thousands)

	Year ended December 31,		
	2016	2015	2014
Operating activities:			
Net loss	$(135,747)	$(60,716)	$(37,034)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	296	96	49
Amortization of premium/discount on investments	494	558	268
Loss on disposal of property and equipment	306	—	—
Stock-based compensation	5,825	4,714	6,010
Changes in operating assets and liabilities:			
Unbilled receivable	(33,823)	—	—
Prepaid expenses and other current assets	428	(1,001)	(686)
Other long-term assets	(2)	(976)	(179)
Accounts payable	(274)	231	1,307
Accrued expense	20,703	4,646	2,754
Deferred revenue	197,289	—	—
Deferred rent	2,411	41	28
Net cash provided by (used in) operating activities	57,906	(52,407)	(27,483)
Investing activities:			
Purchase of equipment	(2,662)	(414)	(229)
Proceeds from the maturities of available for sale securities	162,376	63,901	12,585
Purchase of available for sale securities	(147,009)	(77,175)	(77,708)
Net cash provided by (used in) investing activities	12,705	(13,688)	(65,352)
Financing activities:			
Proceeds from the issuance of common stock, net of issuance costs	66,736	82,750	104,328
Proceeds from the sale of stock under employee stock purchase plan	106	220	—
Proceeds from the exercise of stock options	124	130	—
Repurchase of treasury stock	—	—	(162)
Payments received on promissory notes issued in exchange for shares of common stock	—	—	237
Payments on capital lease obligations	(20)	(7)	(3)
Net cash provided by financing activities	66,946	83,093	104,400
Increase in cash and cash equivalents	137,557	16,998	11,565
Cash and cash equivalents at beginning of the period	49,778	32,780	21,215
Cash and cash equivalents at end of the period	$187,335	$49,778	$32,780
Non-cash financing activities			
Conversion of series A, series B and series C preferred stock into common stock	$—	$—	$244,727
Accretion of preferred stock to redemption value	$—	$—	$86,899

Unpaid follow-on offering costs	$12	$102	$—
Assets acquired under capital lease	$—	$12	$—

See accompanying notes to consolidated financial statements.

Akebia Therapeutics, Inc.

Notes to Consolidated Financial Statements

1. Nature of Organization and Operations

Incorporated in Delaware in 2007, Akebia Therapeutics, Inc. (Akebia, or the Company) is a biopharmaceutical company focused on developing and delivering novel therapeutics for patients based on hypoxia-inducible factor, or HIF, biology, and building our pipeline while leveraging its development and commercial expertise in renal disease. HIF is the primary regulator of the production of red blood cells (RBCs) in the body, as well as other important metabolic functions. Pharmacologic modulation of the HIF pathway may have broad therapeutic applications. The Company's lead product candidate, vadadustat, is a HIF-PH inhibitor in Phase 3 development, which has the potential to set a new standard of care in the treatment of anemia associated with chronic kidney disease (CKD). The Company's management team has extensive experience in developing and commercializing drugs for the treatment of renal and metabolic disorders, as well as a deep understanding of HIF biology. This unique combination of HIF and renal expertise is enabling the Company to advance a pipeline of HIF-based therapies to address serious diseases.

The Company's operations to date have been limited to organizing and staffing the Company, business planning, raising capital, acquiring and developing its technology, identifying potential product candidates and undertaking preclinical and clinical studies. The Company has not generated any product revenue to date and may never generate any product revenue in the future. The Company's product candidates are subject to long development cycles and the Company may be unsuccessful in its efforts to develop, obtain regulatory approval for or market its product candidates.

The Company is subject to a number of risks including, but not limited to, the need to obtain adequate additional funding, including the resources necessary to fund the vadadustat Phase 3 program in non-dialysis dependent (NDD)-CKD, called PRO_2TECT, and dialysis depended (DD) CKD, called $INNO_2VATE$. In December 2015 the first patient was dosed in PRO_2TECT, and the first patient was dosed in $INNO_2VATE$ in August 2016. Overall, the PRO_2TECT and $INNO_2VATE$ Phase 3 programs are designed to enroll approximately 5,700 patients. The Company has engaged Quintiles as our primary CRO for the PRO_2TECT and $INNO_2VATE$ programs. We expect the cost of the PRO_2TECT and $INNO_2VATE$ programs to be in the range of $80,000 to $85,000 per patient, aggregating in the range of $456.0 million to $484.5 million in external CRO costs for the total program. These estimated costs could increase significantly if the Phase 3 program takes longer to complete or if we choose to add additional investigative sites, add additional patients, modify the clinical trial protocol, or perform other studies in support of the Phase 3 program. The enrollment numbers and the completion of the Phase 3 program will be driven by the assessment of major adverse cardiovascular events, or MACE. If the results of the Phase 3 program support the results observed across our previous 15 clinical studies, and the observed event rate is consistent with expectations, the Company anticipates submitting a New Drug Application (NDA) to the Food and Drug Administration (FDA) for vadadustat in the treatment of anemia associated with CKD for each indication in 2019.

The Company is also subject to a number of other risks including possible failure of preclinical testing or clinical trials, the need to obtain marketing approval for its product candidates, the development of new technological innovations by competitors, the need to successfully commercialize and gain market acceptance of any of the Company's products that are approved and uncertainty around intellectual property matters. If the Company does not successfully commercialize any of its products, it will be unable to generate product revenue or achieve profitability.

Through 2016 we have raised approximately $254.1 million of net proceeds from five underwritten public offerings, including $61.0 million of net proceeds raised in January 2016 whereby we sold 7,250,000 shares of common stock at a price of $9.00 per share and $5.7 million of net proceeds whereby we sold 615,293 shares of common in an at-the-market offering, or ATM, pursuant to a Sales Agreement with Cantor Fitzgerald & Co. entered into in May 2016.

In December 2015, the Company entered into a collaboration agreement with Mitsubishi Tanabe Pharma Corporation, or MTPC, to develop and commercialize vadadustat in Japan and certain other countries in Asia for total payments of up to $350.0 million to fund the vadadustat Phase 3 program, including up to $100.0 million in upfront and development payments, of which $40.0 million was received in January 2016. To the extent Japanese patients are included in the Phase 3 Program, MTPC will fund up to an additional $60.0 million of development costs. If Japanese patients are not included in the Phase 3 Program, MTPC will be responsible for the costs of the local Phase 3 study in Japan and will make no additional funding payments for the Phase 3 Program, and $20.0 million of the $40.0 million the Company received in 2016 would be used to fund local development of vadadustat in Japan or be refunded to MTPC, at MTPC’s discretion.

In December 2016, we entered into a collaboration and license agreement with Otsuka to develop and commercialize vadadustat in the United States. In December 2016, we received $125.0 million upfront payment and in March 2017, Otsuka reimbursed us approximately $33.8 million for global expenses previously incurred by us for our ongoing global development program for vadadustat in DD-CKD and NDD-CKD patients. The agreement also provides for additional funding for the global development

program for vadadustat, totaling $106.2 million or more (depending on the actual global development costs incurred). In addition, if the development costs exceed a certain threshold, Akebia may require Otsuka to pay a higher percentage of the global development costs. In such event, Otsuka would be reimbursed for such additional funding out of milestone payments and net sales of vadadustat in the Territory. In addition, Akebia is eligible to receive from Otsuka up to $765.0 million in specified development and commercial milestones. We will share equally with Otsuka the costs of developing and commercializing vadadustat in the United States and the profits from sales of vadadustat after approval by the FDA.

In February 2017, we entered into a Research and License Agreement with Janssen, the Agreement, pursuant to which Janssen granted us an exclusive, license under certain intellectual property rights to develop and commercialize worldwide certain HIF prolyl hydroxylase-targeted compounds.

Under the terms of the Agreement, Janssen granted us a license for a three-year research term to conduct research on the HIF compound portfolio, unless we elect to extend such research term for up to two additional one-year periods upon payment of an extension fee. During the research term, we may designate one or more compounds as candidates for development and commercialization. Once a compound is designated for development and commercialization, we will be solely responsible for the development and commercialization of the compound worldwide at our own cost and expense.

The Agreement includes a license to develop and commercialize JNJ5169, a preclinical compound in development as an oral treatment for inflammatory bowel disease. Under the terms of the Agreement, we will pay an upfront payment of $1.0 million to Janssen within 30 days of execution of the Agreement. In addition, Janssen could be eligible to receive up to an aggregate of $16.5 million from us in specified development milestone payments on a product-by-product basis. Janssen will also be eligible to receive up to $215.0 million from us in specified commercial milestones as well as tiered, escalating royalties ranging from a low to mid-single digit percentage of net sales, on a product-by-product basis.

The Company believes that it can continue as a going concern as its cash resources of approximately $260.3 million at December 31, 2016, together with the committed funding from its collaboration partners, including approximately $33.8 million received from Otsuka in March 2017, will be sufficient to allow the Company to fund its current operating plan into mid-2018, and as a result, through at least twelve months from the filing of the Company’s 2016 annual report on Form 10-K. There can be no assurance, however, that the current operating plan will be achieved in the time frame anticipated by the Company, or that its cash resources will fund the Company’s operating plan for the period anticipated by the Company or that additional funding will be available on terms acceptable to the Company, or at all. We will require additional capital for the further development of our existing product candidates and will need to raise additional funds sooner to pursue development activities related to additional product candidates. If and until we can generate a sufficient amount of revenue from our products, we expect to finance future cash needs through public or private equity, debt offerings, or strategic transactions.

Unless otherwise indicated, all information in these consolidated financial statements gives retrospective effect to the 1.75-for-1 stock split of the Company’s common stock (the Stock Split) that was effected on March 6, 2014 (see Note 6), as well as any other stock-splits in historical periods.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying consolidated financial statements include the accounts of the Company and its wholly-owned subsidiaries, Akebia Therapeutics Securities Corporation and Akebia Europe Limited. All intercompany balances and transactions have been eliminated in consolidation. These condensed consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America (U.S. GAAP). Any reference in these notes to applicable guidance is meant to refer to the authoritative U.S. GAAP as found in the Accounting Standards Codification (ASC) and Accounting Standards Update (ASU) of the Financial Accounting Standards Board (FASB).

In the quarter ended December 31, 2015, the Company identified and corrected an error in the historical classification of certain operating costs between research and development and general and administrative expenses. The Company concluded the effect of this classification error was not material to its consolidated financial statements for any prior period. The classification correction had no effect on the Company’s current or historical total operating expenses or net loss.

Recent Accounting Pronouncements

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 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 March 2016, the FASB issued ASU 2016-09, Improvements to Employee Share-Based Payment Accounting, as part of its Simplification Initiative. The areas for simplification in this update involve several aspects of the accounting for share-based payment transactions, including the income tax consequences, classification of awards as either equity or liabilities, and classification on the statement of cash flows. Some of the areas for simplification apply only to nonpublic entities. The amendments in ASU 2016-09 are effective for fiscal years beginning after December 15, 2016, and interim periods within those fiscal years. Early application is permitted for all entities. The Company is currently evaluating the impact of this new standard on its consolidated financial statements.

In February 2016, the FASB issued ASU 2016-02, Leases (Topic 842), which supersedes the existing guidance for lease accounting, Leases (Topic 840). ASU 2016-02 requires lessees to recognize leases on their balance sheets, and leaves lessor accounting largely unchanged. The amendments in this ASU are effective for fiscal years beginning after December 15, 2018 and interim periods within those fiscal years. Early application is permitted for all entities. ASU 2016-02 requires a modified retrospective approach for all leases existing at, or entered into after, the date of initial application, with an option to elect to use certain transition relief. The Company is currently evaluating the impact of this new standard on its consolidated financial statements.

In November 2015, the FASB issued ASU No. 2015-17, to simplify the presentation of deferred income taxes. The new standard requires that all deferred tax assets and liabilities, along with any related valuation allowance, be classified as noncurrent on the balance sheet. The standard is effective for interim and annual periods beginning after December 15, 2016 and allows for early adoption using a full retrospective method or a prospective method for all periods presented. The Company elected to early adopt the provisions of this new standard in the fourth quarter of 2015 using a full retrospective method. The accounting standard did not have any impact on the Company’s consolidated financial statements since a full valuation allowance has been provided on the Company’s deferred tax assets (see Note 7).

In August 2014, the FASB issued ASU 2014-15, which requires management of public and private companies to evaluate whether there is substantial doubt about the entity’s ability to continue as a going concern within one year after the date that the financial statements are issued. Management’s evaluation should be based on relevant conditions and events that are known and reasonably knowable at the date that the financial statements are issued. If conditions or events raise substantial doubt about an entity’s ability to continue as a going concern, and substantial doubt is not alleviated after consideration of management’s plans, an entity should include a statement in the footnotes indicating that there is substantial doubt about the entity’s ability to continue as a going concern within one year after the date that the financial statements are issued. The new standard is effective for annual periods ending after December 15, 2016, and for annual periods and interim periods thereafter. The Company adopted the standard in the fourth quarter of 2016. See Note 1 for additional information on our liquidity risks and management’s plans.

In May 2014, the FASB, issued a new revenue recognition standard which amends revenue recognition principles and provides a single, comprehensive set of criteria for revenue recognition within and across all industries. The new

standard provides a five step framework whereby revenue is recognized when promised goods or services are transferred to a customer at an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. The standard also requires enhanced disclosures pertaining to revenue recognition in both interim and annual periods. In August 2015, the FASB deferred the effective date of the new revenue standard from January 1, 2017 to January 1, 2018. Early adoption is permitted any time after the original effective date, which for us is January 1, 2017. The Company intends to adopt the new standard on January 1, 2018. The standard allows for adoption using a full retrospective method or a modified retrospective method. The Company's historical revenue has been derived from its collaboration agreements with MTPC and Otsuka. These arrangements contain multiple-elements and have been accounted for pursuant to ASC 605-25. As of December 31, 2016, the Company has not commenced revenue recognition under the MTPC arrangement as the Company is not yet able to determine all of its deliverables and the total amount of arrangement consideration. The new revenue standard provides guidance in assessing what comprises the distinct service being provided to a customer that may have implications to our performance obligations and unit of account identified in our two existing collaborations which could be defined differently under the new guidance. As a result, there could be changes to the timing of revenue recognition upon adoption of the new standard. The Company is currently assessing the impact of the new revenue recognition standard on its two collaboration agreements and evaluating which method it will use to adopt.

Segment Information

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision maker, or decision-making group, in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business in one operating segment, which is the business of developing and commercializing proprietary therapeutics based on HIF biology.

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results may differ from those estimates. 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 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. Estimates are used in the following areas, among others: prepaid and accrued research and development expense, stock-based compensation expense, accrued expenses, revenue and income taxes.

Prior to the initial public offering, the Company utilized significant estimates and assumptions in determining the fair value of its common stock. The Company granted stock options at exercise prices not less than the fair market value of its common stock as determined by the Board of Directors contemporaneously at the date such grants were made, with input from management. Prior to the Company's initial public offering in March 2014, the fair value of common stock at the grant date was adjusted in connection with the Company's retrospective fair value assessment for financial reporting purposes. Accordingly, the Board of Directors determined the estimated fair value of the Company's common stock based on a number of objective and subjective factors, including external market conditions affecting the biotechnology industry sector and the prices at which the Company sold shares of preferred stock, the superior rights and preferences of securities senior to the Company's common stock at the time and the likelihood of achieving a liquidity event, such as an initial public offering or sale of the Company.

The Company utilized various valuation methodologies in accordance with the framework of the American Institute of Certified Public Accountants Technical Practice Aid, Valuation of Privately-Held Company Equity Securities Issued as Compensation, to estimate the fair value of its common stock in periods prior to March 2014. The methodologies included a probability analysis including both a potential public trading scenario and potential sale scenario. In both scenarios, value is estimated using the guideline public company method. The sale scenario includes an adjustment for a market participant acquisition premium. Value is allocated among the preferred and common shares according to the rights associated with each type of security. Valuation methodologies include estimates and assumptions that require the Company's judgment. These estimates include assumptions regarding future performance, including the successful completion of a public offering. Significant changes to the key assumptions used in the valuations could result in different fair values of common stock at each valuation date.

Cash and Cash Equivalents

Cash and cash equivalents consist of all cash on hand, deposits and funds invested in available-for-sale securities with original maturities of three months or less at the time of purchase. At December 31, 2016, the Company's cash is primarily in money market funds. The Company may maintain balances with its banks in excess of federally insured

limits.

Investments

Management determines the appropriate classification of securities at the time of purchase and reevaluates such designation as of each balance sheet date. Currently, the Company classifies all securities as available-for-sale which are included in current assets as they are intended to fund current operations. The Company carries available-for-sale securities at fair value. The Company conducts periodic reviews to identify and evaluate each investment that has an unrealized loss, in accordance with the meaning of other-than-temporary impairment and its application to certain investments. When assessing whether a decline in the fair value of a security is other-than-temporary, the Company considers the fair market value of the security, the duration of the security's decline, and prospects for the underlying business. Based on these considerations, the Company did not identify any other-than-temporary unrealized losses at December 31, 2016. Unrealized losses on available-for-sale securities that are determined to be temporary, and not related to credit loss, are recorded in accumulated other comprehensive loss, a component of stockholders' equity. The amortized cost of debt securities in this category reflects amortization of premiums and accretion of discounts to maturity computed under the

effective interest method. The Company includes this amortization in the caption “Interest income” within the consolidated statements of operations and comprehensive loss. The Company also includes in net investment income, realized gains and losses and declines in value determined to be other than temporary. The Company bases the cost of securities sold upon the specific identification method, and includes interest and dividends on securities in interest income.

Revenue Recognition

To date, the Company has not generated any revenue from the sales of products. For the foreseeable future, the Company expects substantially all of its revenues will be generated from its collaborations with MTPC and Otsuka (see Note 9) and any other collaborations the Company may enter into.

Multiple-Element Arrangements

The Company recognizes revenue in accordance with ASC Topic 605, Revenue Recognition (ASC 605). Accordingly, revenue is recognized for each unit of accounting when all of the following criteria are met:

- Persuasive evidence of an arrangement exists;
- Delivery has occurred or services have been rendered;
- The seller’s price to the buyer is fixed or determinable; and
- Collectability is reasonably assured.

Amounts received prior to satisfying the revenue recognition criteria are recorded as deferred revenue. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified in current liabilities. 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.

Revenue recognition from our MTPC collaboration will commence when all criteria as required under SC 605 have been satisfied. Therefore, collaboration revenue in 2016 is generated exclusively from its collaboration arrangement with Otsuka. The terms of this arrangement contain multiple deliverables, which include at inception: (i) license, (ii) development services, (iii) rights to future intellectual property and (iv) joint committee services. Non-refundable payments to the Company under this arrangement include: (i) up-front fee, (ii) payments for development services and (iii) payments based on the achievement of certain milestones. Also, the Company and Otsuka share costs incurred with respect to jointly conducted medical affairs and commercialization and non-promotional activities under the collaboration. Additionally, the Company may receive its share of net sales and bear its share of shared costs from the sale of products containing or comprising vadadustat in the United States through its collaboration with Otsuka. The Company will recognize revenue related to amounts allocated to the License Unit of Accounting on a proportional performance basis as the underlying services are performed.

The Company evaluates multiple element arrangements based on the guidance in ASC Topic 605 25, Revenue Recognition Multiple Element Arrangements (ASC 605 25). Pursuant to the guidance in ASC 605 25, the Company evaluates multiple element arrangements to determine (i) the deliverables included in the arrangement and (ii) whether the individual deliverables represent separate units of accounting or whether they must be accounted for as a combined unit of accounting. This evaluation involves subjective determinations and requires the Company to make judgments about the individual deliverables and whether such deliverables are separable from the other aspects of the contractual relationship. Deliverables are considered separate units of accounting provided that: (i) the delivered item(s) has value to the customer on a standalone basis and (ii) if the arrangement includes a general right of return relative to the delivered item(s), delivery or performance of the undelivered item(s) is considered probable and substantially in the Company’s control. In assessing whether an item has standalone value, the Company considers factors such as the research, development, manufacturing and commercialization capabilities of the collaboration

partner and the availability of the associated expertise in the general marketplace. In addition, the Company considers whether the collaboration partner can use the other deliverable(s) for their intended purpose without the receipt of the remaining deliverable(s), whether the value of the deliverable is dependent on the undelivered item and whether there are other vendors that can provide the undelivered item(s). The Company's collaboration arrangements do not contain a general right of return relative to delivered item(s).

Arrangement consideration that is fixed or determinable is allocated among the separate units of accounting using the relative selling price method. The Company determines the selling price for a unit of accounting following the hierarchy of evidence prescribed by ASC 605-25. Accordingly, the Company determines the estimated selling price for units of accounting within each arrangement using vendor specific objective evidence (VSOE) of selling price, if available, third party evidence (TPE) of selling price if VSOE is not available, or best estimate of selling price (BESP) if neither VSOE nor TPE is available. Determining the BESP for a unit of

accounting requires significant judgment. In developing the BESP for a unit of accounting, the Company considers applicable market conditions and relevant entity specific factors, including factors that were contemplated in negotiating the agreement with the customer and estimated costs. The Company validates the BESP for units of accounting by evaluating whether changes in the key assumptions used to determine the BESP will have a significant effect on the allocation of arrangement consideration between multiple units of accounting.

The Company recognizes arrangement consideration allocated to each unit of accounting when all of the revenue recognition criteria in ASC 605 are satisfied for that particular unit of accounting. The Company recognizes as revenue arrangement consideration attributed to licenses that have standalone value from other deliverables to be provided in an arrangement upon delivery. The Company recognizes as revenue arrangement consideration attributed to licenses that do not have standalone value from the other deliverables to be provided in an arrangement over the contractual or estimated performance period associated with the undelivered elements included in the combined unit of accounting, which is typically the term of the Company's development obligations. If there is no discernible pattern of performance and/or objectively measurable performance measures do not exist, then the Company recognizes revenue under the arrangement on a straight line basis over the period the Company is expected to complete its performance obligations. Conversely, if the pattern of performance in which the service is provided to the customer can be determined and objectively measurable performance measures exist, then the Company recognizes revenue under the arrangement using the proportional performance method. Revenue recognized is limited to the lesser of the cumulative amount of payments received or the cumulative amount of revenue earned, as determined using the straight line method or proportional performance method, as applicable, as of the period ending date.

The Company recognizes associated with milestones in accordance with the provisions of ASC Topic 605-28, Revenue Recognition-Milestone Method. Accordingly, at the inception of an arrangement that includes milestone payments, the Company evaluates whether each milestone is substantive and at risk to both parties on the basis of the contingent nature of the milestone. This evaluation includes an assessment of whether: (i) the consideration is commensurate with either the Company's performance to achieve the milestone or the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from its performance to achieve the milestone, (ii) the consideration relates solely to past performance and (iii) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. The Company evaluates factors such as the scientific, clinical, regulatory, commercial, and other risks that must be overcome to achieve the respective milestone and the level of effort and investment required to achieve the respective milestone in making this assessment. There is considerable judgment involved in determining whether a milestone satisfies all of the criteria required to conclude that a milestone is substantive. Milestones that are considered substantive are recognized as revenue in their entirety upon achievement, assuming all other revenue recognition criteria are met. Milestones that are not considered substantive are recognized as revenue upon achievement if there are no remaining performance obligations or over the remaining period of performance if there are remaining performance obligations, assuming all other revenue recognition criteria are met. Revenue from commercial milestone payments will be accounted for as royalties and recorded as revenue upon achievement of the milestone, assuming all other revenue recognition criteria are met.

The Company will recognize royalty revenue in the period of sale of the related product(s), based on the underlying contract terms, provided that the reported sales are reliably measurable and the Company has no remaining performance obligations, assuming all other revenue recognition criteria are met.

Collaborative Arrangements

The Company records the elements of its collaboration agreements that represent joint operating activities in accordance with ASC Topic 808, Collaborative Arrangements (ASC 808). Accordingly, the elements of the collaboration agreements that represent activities in which both parties are active participants and to which both parties are exposed to the significant risks and rewards that are dependent on the commercial success of the activities

are recorded as collaborative arrangements. The Company considers the guidance in ASC Topic 605-45, Revenue Recognition—Principal Agent Considerations (ASC 605-45) in determining the appropriate treatment for the transactions between the Company and its collaborative partner and the transactions between the Company and third parties. Generally, the classification of transactions under the collaborative arrangements is determined based on the nature and contractual terms of the arrangement along with the nature of the operations of the participants. The Company recognizes its allocation of the shared costs incurred with respect to the jointly conducted medical affairs and commercialization and non-promotional activities under the collaboration with Otsuka as a component of the related expense in the period incurred. To the extent revenue is generated from the collaboration, the Company will recognize its share of the net sales on a gross basis if it is deemed to be the principal in the transactions with customers, or on a net basis if it is instead deemed to be the agent in the transactions with customers, consistent with the guidance in ASC 605-45.

Patents

Costs incurred in connection with the application for and issuance of patents are expensed as incurred.

Income Taxes

Income taxes are recorded in accordance with FASB 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 elected to early adopt the provisions of ASU No. 2015-17 in the fourth quarter of 2015 using a full retrospective method. As a result, all deferred taxes as of December 31, 2016 and 2015 are classified as noncurrent within the income tax provision (see Note 7), however as we record a full valuation allowance against the Company's net deferred tax assets, the adoption of this standard has no impact on our consolidated balance sheets as of December 31, 2016 and 2015.

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, 2016 and 2015, the Company does not have any significant uncertain tax positions. The Company recognizes interest and penalties related to uncertain tax positions in income tax expense.

Stock-Based Compensation

The Company accounts for its stock-based compensation awards in accordance with FASB ASC Topic 718, Compensation—Stock Compensation (ASC 718). ASC 718 requires all stock-based payments to employees, including grants of employee stock options, restricted stock, restricted stock units, or RSUs, and modifications to existing stock awards, to be recognized in the statements of operations and comprehensive loss based on their fair values. The Company accounts for stock-based awards to non-employees in accordance with FASB ASC Topic 505-50, Equity-Based Payments to Non-Employees (ASC 505-50), which requires the fair value of the award to be re-measured at fair value until a performance commitment is reached or counterparty performance is complete. The Company's stock-based awards are comprised of stock options, shares of restricted stock and shares of common stock. The Company estimates the fair value of options granted using the Black-Scholes option pricing model. The Company uses the quoted market price of comparable public companies to determine the fair value of restricted stock awards and common stock awards.

The Black-Scholes option pricing model requires the input of certain subjective assumptions, including (a) the expected stock price volatility, (b) the calculation of expected term of the award, (c) the risk-free interest rate and (d) expected dividends. Due to the lack of company-specific historical and implied volatility data for trading the Company's stock in the public market, the Company has based its estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. The historical volatility is calculated based on a period of time commensurate with the expected term assumption. The computation of expected volatility is based on the historical volatility of a representative group of companies with similar characteristics to the Company, including stage of product development and life science industry focus. The Company is in the product development stage with no revenue and the representative group of companies has certain similar characteristics to the Company. The Company believes the group selected has sufficient similar economic and industry characteristics, and includes companies that are most representative of the Company. The Company uses the simplified method as prescribed by the SEC Staff Accounting Bulletin No. 107, Share-Based Payment, to calculate the expected term for options granted to employees as it does not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. The expected term is applied to the stock option grant group as a whole, as the Company

does not expect substantially different exercise or post-vesting termination behavior among its employee population. For options granted to non-employees, the Company utilizes the contractual term of the arrangement as the basis for the expected term assumption. The risk-free interest rate is based on a treasury instrument whose term is consistent with the expected life of the stock options. The expected dividend yield is assumed to be zero as the Company has never paid dividends and has no current plans to pay any dividends on its common stock, which is similar to the Company's peer group.

The Company's stock-based awards are subject to service based vesting conditions. Compensation expense related to awards to employees with service-based vesting conditions is recognized on a straight-line basis based on the grant date fair value over the associated service period of the award, which is generally the vesting term. Consistent with the guidance in ASC 505- 50, compensation expense related to awards to non-employees with service-based vesting conditions is recognized on a straight-line basis based on the then-current fair value at each financial reporting date prior to the measurement date over the associated service period of the award, which is generally the vesting term.

The Company is also required to estimate forfeitures at the time of grant, and revise those estimates in the subsequent periods if actual forfeitures differ from its estimates. The Company uses historical data to estimate pre-vesting forfeitures and record stock-based

compensation expense only for those awards that are expected to vest. To the extent that actual forfeitures differ from the Company's estimates, the difference is recorded as a cumulative adjustment in the period the estimates were revised. Stock-based compensation expense recognized in the condensed consolidated financial statements is based on awards that are ultimately expected to vest.

Fair Value of Financial Instruments

The Company is required to disclose information on all assets and liabilities reported at fair value that enables an assessment of the inputs used in determining the reported fair values. FASB ASC Topic 820, Fair Value Measurements and Disclosures (ASC 820), establishes a hierarchy of inputs used in measuring fair value that maximizes the use of observable inputs and minimizes the use of unobservable inputs by requiring that the observable inputs be used when available.

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. The fair value hierarchy applies only to the valuation inputs used in determining the reported fair value of the investments, and is not a measure of the investment credit quality. The three levels of the fair value hierarchy are described below:

- Level 1 – Valuations based on unadjusted quoted prices in active markets for identical assets or liabilities that the Company has the ability to access at the measurement date.
- Level 2 – Valuations based on quoted prices for similar assets or liabilities in markets that are not active, or for which all significant inputs are observable, either directly or indirectly.
- Level 3 – Valuations that require inputs that reflect the Company's own assumptions that are both significant to the fair value measurement and unobservable.

To the extent that 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 investments (see Note 4). The carrying amounts of prepaid expenses and other current assets, accounts payable and accrued expenses approximate their fair values due to their short-term maturities. The rate implicit within the Company's capital lease obligation approximates market interest rates.

Concentrations of Credit Risk and Off-Balance Sheet Risk

Cash and investments are the only financial instruments that potentially subject the Company to concentrations of credit risk. The Company maintains its cash with high quality, accredited financial institutions and, accordingly, such funds are subject to minimal credit risk. The Company has no significant off-balance sheet concentrations of credit risk, such as foreign currency exchange contracts, option contracts or other hedging arrangements.

Net Loss per Share

Basic net loss per share is calculated by dividing net loss attributable to common stockholders by the weighted-average shares outstanding during the period, without consideration for common stock equivalents. Diluted net loss per share is calculated by adjusting weighted-average shares outstanding for the dilutive effect of common stock equivalents outstanding for the period, determined using the treasury-stock method. For purposes of the diluted

net loss per share calculation, preferred stock, stock options, unvested restricted stock and RSUs are considered to be common stock equivalents, but have been excluded from the calculation of diluted net loss per share, as their effect would be anti-dilutive for all periods presented. Therefore, basic and diluted net loss per share were the same for all periods presented.

Property and Equipment

Property and equipment is stated at cost, less accumulated depreciation. Assets under capital lease are included in property and equipment. Property and equipment is depreciated using the straight-line method over the estimated useful lives of the assets, generally three to seven years. Such costs are periodically reviewed for recoverability when impairment indicators are present. Such indicators include, among other factors, operating losses, unused capacity, market value declines and technological obsolescence. Recorded values of asset groups of equipment that are not expected to be recovered through undiscounted future net cash flows are

written down to current fair value, which generally is determined from estimated discounted future net cash flows (assets held for use) or net realizable value (assets held for sale).

The following is the summary of property and equipment and related accumulated depreciation as of December 31, 2016 and 2015.

	Useful Life	December 31, 2016	December 31, 2015
		(in thousands)	
Computer equipment and software	3	$476	$ 300
Furniture and fixtures	5	729	243
Equipment	7	50	50
Leasehold improvements	Shorter of the useful life or remaining lease term (10 years)	1,763	70
Office equipment under capital lease	3	36	24
		3,054	687
Less accumulated depreciation		(442)	(147)
Net property and equipment		$2,612	$ 540

Depreciation expense, including expense associated with assets under capital leases, was approximately $295,000, $96,000 and $49,000 for the years ended December 31, 2016, 2015 and 2014, respectively.

3. Available for sale securities

Available for sale securities at December 31, 2016 and 2015 consist of the following:

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
	(in thousands)			
December 31, 2016				
Cash and cash equivalents	$187,335	$ —	$ —	$187,335
Available for sale securities:				

Certificates of deposit	$12,698	—	—	$12,698
U.S. Government debt securities	50,952	—	(32)	50,920
Corporate debt securities	9,398	—	(8)	9,390
Total available for sale securities	$73,048	$ —	$ (40)	$73,008
Total cash, cash equivalents, and available for sale securities	$260,383	$ —	$ (40)	$260,343

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
	(in thousands)			
December 31, 2015				
Cash and cash equivalents	$49,778	$ —	$ —	$49,778
Available for sale securities:				
Certificates of deposit	$21,505	—	—	$21,505
U.S. Government debt securities	46,461	—	(185)	46,276
Corporate debt securities	20,944	1	(50)	20,895
Total available for sale securities	$88,910	$ 1	$ (235)	$88,676
Total cash, cash equivalents, and available for sale securities	$138,688	$ 1	$ (235)	$138,454

The estimated fair value of the Company's available-for-sale securities balance at December 31, 2016, by contractual maturity, is as follows:

Due in one year or less	$65,071
Due after one year	7,937
Total available for sale securities	$73,008

4. Fair Value of Financial Instruments

The Company utilizes a portfolio management company for the valuation of the majority of its investments. This company is an independent, third-party vendor recognized to be an industry leader with access to market information that obtains or computes fair market values from quoted market prices, pricing for similar securities, recently executed transactions, cash flow models with yield curves and other pricing models. For valuations obtained from the pricing service, the Company performs due diligence to understand how the valuation was calculated or derived, focusing on the valuation technique used and the nature of the inputs.

Based on the fair value hierarchy, the Company classifies its cash equivalents and available-for-sale securities within Level 1 or Level 2. This is because the Company values its cash equivalents and available-for-sale securities using quoted market prices or alternative pricing sources and models utilizing market observable inputs.

Assets measured or disclosed at fair value on a recurring basis as of December31, 2016 are summarized below:

	Fair Value Measurements Using			
	Level 1	Level 2	Level 3	Total
	(in thousands)			
December 31, 2016				
Assets:				
Cash and cash equivalents	$187,335	$—	$ —	$187,335
Certificates of deposit	—	12,698	—	12,698
U.S. Government debt securities	—	50,920	—	50,920
Corporate debt securities	—	9,390	—	9,390
	$187,335	$73,008	$ —	$260,343

Assets measured or disclosed at fair value on a recurring basis as of December 31, 2015 are summarized below:

	Fair Value Measurements Using			
	Level 1	Level 2	Level 3	Total
	(in thousands)			
December 31, 2015				

Assets:				
Cash and cash equivalents	$49,778	$—	$ —	$49,778
Certificates of deposit	—	21,505	—	21,505
U.S. Government debt securities	—	46,276	—	46,276
Corporate debt securities	—	20,895	—	20,895
	$49,778	$88,676	$ —	$138,454

The Company’s corporate debt securities are all investment grade.

The Company had no assets or liabilities measured at fair value on a recurring basis using significant unobservable inputs (Level 3) at December 31, 2016 and December 31, 2015.

Investment securities are exposed to various risks such as interest rate, market and credit. Due to the level of risk associated with certain investment securities and the level of uncertainty related to changes in the value of investment securities, it is at least reasonably possible that changes in risks in the near term would result in material changes in the fair value of investments.

5. Accrued Expenses

Accrued expenses are as follows:

	December 31, 2016	December 31, 2015
	(in thousands)	
Accrued clinical	$23,643	$ 4,536
Accrued bonus	2,995	2,178
Accrued payroll	596	518
Professional fees	539	647
Accrued vacation	513	310
Accrued severance	29	—
Other	1,946	1,366
Total accrued expenses	$30,261	$ 9,555

During 2016, the Company entered into separation agreements with three employees. During 2016, the Company recorded severance expense in the amount of $0.5 million, of which $0.2 million was recorded to general and administrative expense and $0.3 million was recorded to research and development expense. During the year ended December 31, 2016, approximately $0.4 million was paid out of the severance accrual. At December 31, 2016, approximately $29,000 remained in accrued expense in relation to the unpaid severance costs.

6. Stockholders' Equity

Authorized and Outstanding Capital Stock

As of December 31, 2014, the authorized capital stock of the Company included 175,000,000 shares of common stock, par value $0.00001 per share, of which 38,615,709 and 30,662,218 shares are issued and outstanding at December 31, 2016 and 2015, respectively; and 25,000,000 shares of undesignated preferred stock, par value $0.00001 per share, of which 0 shares are issued and outstanding at December 31, 2016 and December 31, 2015.

On March 6, 2014, the Company effected a 1.75-for-1 stock split of its outstanding common stock. Unless otherwise indicated, all share data and per share amounts in these financial statements have been retroactively adjusted to reflect the stock split, as well as any stock splits that occurred in periods prior to March 6, 2014.

Upon the closing of the IPO on March 25, 2014, all of the outstanding shares of the Company's redeemable convertible preferred stock were converted into 12,115,183 shares of its common stock. As of December 31, 2014, the Company does not have any redeemable convertible preferred stock issued or outstanding.

Equity Plans

On February 28, 2014, the Company's Board of Directors adopted its 2014 Incentive Plan (the "2014 Plan") and its 2014 Employee Stock Purchase Plan (the "ESPP"), which were subsequently approved by its stockholders and became effective upon the closing of the Company's initial public offering IPO on March 25, 2014. The 2014 Plan replaced the 2008 Equity Incentive Plan (as amended, the "2008 Plan"), however, options or other awards granted under the 2008 Plan prior to the adoption of the 2014 Plan that have not been settled or forfeited remain outstanding and effective. In May 2016 the Company's Board of Directors approved an inducement award program that was separate from the Company's equity plans and which, consistent with NASDAQ listing rules, did not require shareholder approval (the 2016 program and similar programs, each and "Inducement Award Program") under which 350,000 shares were reserved to be issued in 2016 and 255,000 shares were granted and remain eligible to vest. The Company expects to continue to grant inducement awards to new hires under a 2017 authorization.

The 2014 Plan allows for the granting of stock options, stock appreciation rights (SARs), restricted stock, unrestricted stock, stock units, performance awards and other awards convertible into or otherwise based on shares of our common stock. Dividend equivalents may also be provided in connection with an award under the 2014 Plan. The Company's employees, officers, directors and consultants and advisors are eligible to receive awards under the 2014 Plan. The Company initially reserved 1,785,000 shares of its common stock for the issuance of awards under the 2014 Plan. The 2014 Plan provides that the number of shares reserved and available for issuance under the 2014 Plan will automatically increase annually on January 1st of each calendar year, by an amount equal to three percent (3%) of the number of shares of stock outstanding on a fully diluted basis as of the close of business on the immediately preceding December 31st (the "2014 Plan Evergreen Provision"). The Company's Board of Directors may act prior to January 1st of any year to

provide that there will be no automatic increase in the number of shares available for grant under the 2014 Plan for that year (or that the increase will be less than the amount that would otherwise have automatically been made). During the year ended December 31, 2016, the Company granted 1,304,275 stock options to employees, of which 255,000 shares were under the Inducement Award Program, 450,838 restricted stock units (RSUs) to employees and 112,500 stock options to directors under the 2014 Plan.

The ESPP provides for the issuance of options to purchase shares of the Company's common stock to participating employees at a discount to their fair market value. The maximum aggregate number of shares of common stock available for purchase pursuant to the exercise of options granted under the ESPP will be the lesser of (a) 262,500 shares, increased on each anniversary of the adoption of the ESPP by one percent (1%) of the total shares of common stock then outstanding (the "ESPP Evergreen Provision") and (b) 739,611 shares (which is equal to five percent (5%) of the total shares of common stock outstanding on the date of the adoption of the ESPP on a fully diluted, as converted basis. Under the ESPP, each offering period is six months, at the end of which employees may purchase shares of common stock through payroll deductions made over the term of the offering. The per-share purchase price at the end of each offering period is equal to the lesser of 85% of the closing price of our common stock at the beginning or end of the offering period.

Shares Reserved for Future Issuance

The Company has reserved for future issuance the following number of shares of common stock:

	December 31, 2016	December 31, 2015
Common stock options and RSU's outstanding	3,579,694	2,231,057
Shares available for issuance under the 2014 Plan [1]	885,328	1,318,732
Shares available for issuance under the ESPP [2]	803,105	440,304
Total	5,268,127	3,990,093

[1] On January 1, 2017 and January 1, 2016, the shares reserved for future grants under the 2014 Plan increased by 1,265,863 and 986,800 shares, respectively, pursuant to the 2014 Plan Evergreen Provision.

[2] On February 28, 2017 and February 28, 2016, the shares reserved for future issuance under the ESPP increased by 388,296 and 379,430 shares, respectively, pursuant to the ESPP Evergreen Provision.

Stock-Based Compensation

Stock Options

On February 22, 2016, as part of the Company's annual grant of equity, the Company issued 624,275 stock options to employees. In addition, the Company issues stock options to new hires and occasionally to other employees not in connection with the annual grant process. Options granted by the Company vest over periods of between 12 and 48 months, subject, in each case, to the individual's continued service through the applicable vesting date. Options vest in installments of (i) 25% at the one year anniversary and (ii) in either 36 or 48 equal monthly or 12 equal quarterly installments beginning in the thirteenth month after the initial vesting commencement date or grant date, subject to the individual's continuous service with the Company. Options generally expire ten years after the date of grant. The Company recorded approximately $4.7 million of stock-based compensation expense related to stock options during 2016.

The assumptions used in the Black-Scholes pricing model to estimate the grant date fair value of options granted to employees are as follows:

	Year ended December 31,		
	2016	2015	2014
Risk-free interest rate	1.16% - 2.03%	1.44% - 1.95%	1.63% - 2.06%
Dividend yield	0.00%	0.00%	0.00%
Volatility	64.78% - 82.40%	62.47% - 81.25%	67.97% - 77.00%
Expected term (years)	5.51 - 6.25	5.51 - 6.25	6.25

The following table summarizes the Company's stock option activity:

	Shares	Weighted-Average Exercise Price	Weighted-Average Contractual Life (in years)	Aggregate Intrinsic Value
Outstanding, December 31, 2015	2,206,635	$ 9.04		$13,114,811
Granted	1,416,775	$ 8.11		
Exercised	(86,625)	$ 1.43		$623,686
Forfeited	(388,779)	$ 8.24		$267,459
Expired/cancelled	—			
Outstanding, December 31, 2016	3,148,006	$ 8.93	8.06	$10,437,947
Options exercisable, December 31, 2016	1,134,870	$ 8.34	6.64	$5,785,199
Expected to vest, December 31, 2016	2,805,675	$ 9.31	8.27	$8,759,055

As of December 31, 2016, there was approximately $9.6 million of unrecognized compensation cost related to stock options under the Company's 2014 Plan or made pursuant to the 2016 Inducement Award Program, which is expected to be recognized over a weighted average period of 2.46 years.

Restricted Stock

On December 23, 2013, the Company issued 450,224 shares of restricted stock to employees and 79,067 shares of restricted stock to non-employees at a grant date fair value of $7.42 per share. The aggregate grant date fair value for the shares of restricted stock issued on December 23, 2013 totaled approximately $3.9 million. The awards of restricted stock contained a performance condition wherein vesting is contingent upon the Company's consummation of a liquidity event, as defined, prior to the fifth anniversary of the date of grant. Certain of the awards of restricted stock have a requisite service period that was complete upon grant. The remainder of the awards of restricted stock have a requisite service period of four years whereby the award vests 25% on the one year anniversary of the a specified vesting commencement date, then ratably on the first day of each calendar quarter for 12 quarters, subject to continuous service by the individual and achievement of the performance target. Due to the nature of the performance condition, the Company had concluded that the performance condition was not probable of achievement and therefore, recognition of compensation cost had been deferred until the occurrence of a liquidity event, as defined. Compensation expense related to the restricted stock awards is being recognized over the associated requisite service period which commenced on March 25, 2014, as a result of our IPO. The Company recorded approximately $0.3 million of stock-based compensation expense related to restricted stock during 2016, of which approximately $3,000 was as a result of mark to market adjustments related to non-employees.

A summary of the Company's restricted stock activity is as follows:

	Shares	Weighted-Average Grant Date Fair Value
Restricted shares as of December 31, 2015	216,716	$ 7.80
Granted	—	
Vested	(108,688)	$ 7.71
Forfeited	(15,056)	$ 7.42
Restricted shares as of December 31, 2016	92,972	$ 8.08

As of December 31, 2016, there was approximately $48,000 of unrecognized compensation cost related to the restricted stock awards granted on December 23, 2013 with a performance condition. The recognition of the compensation cost for these awards did not begin until the closing of the initial public offering on March 25, 2014. The unrecognized compensation cost is expected to be recognized over a weighted average period of 0.56 years.

Restricted Stock Units

On February 22, 2016, as part of the Company’s annual grant of equity, the Company issued 382,338 RSUs to employees. In addition, the Company occasionally issues RSUs not in connection with the annual grant process to employees. 100% of each RSU grant vests on the third anniversary of the grant date, subject, in each case, to the individual’s continued service through the applicable vesting

date. Total stock-compensation expense to be recognized over the life of the RSUs is $2.9 million and will be recognized on a straight-line basis over the vesting period. The Company recorded approximately $0.8 million of stock-based compensation expense related to the RSUs in 2016 .

	Shares	Weighted-Average Grant Date Fair Value
Unvested balance, December 31, 2015	24,425	$ 11.15
Granted	450,838	$ 7.83
Vested	—	
Forfeited	(43,575)	$ 8.38
Outstanding, December 31, 2016	431,688	$ 7.96

As of December 31, 2016, there was approximately $2.0 million of unrecognized compensation cost related to RSUs, which is expected to be recognized over a weighted average period of 2.11 years.

Employee Stock Purchase Plan

The first offering period under the ESPP opened on January 2, 2015. There were 16,629 shares issued during the year ended December 31, 2016. The Company recorded approximately $0.1 million of stock-based compensation expense related to the ESPP during 2016.

Compensation Expense Summary

The Company has recognized the following compensation cost related to share-based awards:

	Years ended December 31,		
	2016	2015	2014
	(in thousands)		
Research and development	$2,136	$2,079	$2,766
General and administrative	3,689	2,635	3,244
Total	$5,825	$4,714	$6,010

Compensation expense by type of award:

	Years ended December 31,		
	2016	2015	2014
	(in thousands)		
Stock options	$4,674	$3,660	$1,925
Restricted stock	266	909	4,085
Restricted stock units	780	62	—
Employee stock purchase plan	105	83	—
Total	$5,825	$4,714	$6,010

Included in the compensation expense for the year ended December 31, 2014, is approximately $1.0 million related to the modification of awards in connection with an employee separation agreement in the first quarter of 2014.

7. Income Taxes

The Company's income tax provision was computed based on the federal statutory rate and the state statutory rates, net of the related federal benefit. There was no current or deferred income tax expense or benefit for the years ended December 31, 2016, 2015 and 2014 due to the Company's net losses and increases in its deferred tax asset valuation allowance. The U.S components of loss before income taxes and a reconciliation of the statutory federal income rate to with the provision for income taxes follow:

	Year ended December 31,		
	2016	2015	2014
Federal tax at statutory rate	34.0 %	34.0 %	34.0 %
State and local tax at statutory rate	1.4	3.0	5.5
Research and development tax credits	6.4	0.4	(0.6)
Equity compensation	(0.2)	(0.6)	(1.6)
Other permanent differences and credits	—	—	(0.1)
Change in valuation allowance	(41.6)	(36.8)	(37.2)
Effective tax rate	0.0 %	0.0 %	0.0 %

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. When realization of the deferred tax asset is more likely than not to occur, the benefit related to the deductible temporary differences attributable to operations is recognized as a reduction of income tax expense. Valuation allowances are provided against deferred tax assets when, based on all available evidence, it is considered more likely than not that some portion or all of the recorded deferred tax assets will not be realized in future periods. The Company cannot be certain that future taxable income will be sufficient to realize its deferred tax assets, and accordingly a full valuation allowance has been provided on its deferred tax assets. The Company continues to maintain the underlying tax benefits to offset future taxable income and to monitor the need for a valuation allowance based on the profitability of its future operations. The valuation allowance increased by approximately $56.4 million and 22.3 million, during the years ended December 31, 2016 and 2015. Significant components of the Company's deferred tax assets and liabilities are as follows:

	December 31,	
	2016	2015
	(in thousands)	
Deferred tax assets:		
Accrued expenses	$2,170	$912
Deferred revenue	12,157	—
Intangible assets	449	527
Restricted stock	45	301
Fixed assets	—	—
Non-qualified stock options	2,963	1,558
Research and development credits	10,510	1,829
Net operating loss carryforward	84,372	51,356
Other	326	64
Total deferred tax assets	112,992	56,547

Less valuation allowance	(112,986)	(56,545)
Total deferred tax assets, net of valuation allowance	6	2
Deferred tax liabilities:		
Fixed assets	(6)	(2)
Total deferred tax liabilities	(6)	(2)
Net deferred tax asset	$—	$—

At December 31, 2016 and December 31, 2015, the Company has approximately $0.9 million (after amortization of $1.0 million) and $1.0 million (after amortization of $0.9 million), respectively, of start-up expenses capitalized for income tax purposes with amortization available to offset future federal, state and local income tax. At December 31, 2016 and 2015, the Company has approximately $234.5 million and $140.5 million, respectively, of federal net operating loss (NOL) carry-forwards which expire through 2036. Additionally, at December 31, 2016 and 2015, the Company has approximately $103.9 million and $111.9 million, respectively, of state net operating loss (NOL) carry-forwards which expire through 2036. Included in the 2016 and 2015 NOLs are tax deductions related to equity compensation in excess of book compensation expense. Pursuant to the realization requirements in ASC 718, these tax deductions are not

included in the NOL deferred tax asset above. The Company also has approximately $10.8 million of federal and state research and development tax credit carry-forwards. The NOL and research and development tax credit carry-forwards which expire through 2036, will be utilized for tax purposes at such time the Company generates taxable income. The NOL and research and development tax credit carry-forwards may be limited in certain circumstances, including ownership changes.

Under the provisions of the Internal Revenue Code, the net operating loss and tax credit carry-forwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. Net operating loss and tax credit carryforwards may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant shareholders over a three-year period in excess of 50%, as defined under Sections 382 and 383 of the Internal Revenue Code, respectively, as well as similar state provisions. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the value of the Company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. The Company has completed several financings since its inception, which may have resulted in a change in control as defined by Sections 382 and 383 of the Internal Revenue Code, or could result in a change in control in the future. The Company has not yet analyzed whether there has been a change in control.

For applicable years, the Company generated research credits but has not conducted a study to document its qualified activities. This study may result in an adjustment to the Company’s research and development credit carryforwards; however, until a study is completed and any adjustment is known, no amounts are being presented as an uncertain tax position. A full valuation allowance has been provided against the Company’s research and development credits and, if an adjustment is required, this adjustment would be offset by an adjustment to the deferred tax asset established for the research and development credit carry-forwards and the valuation allowance.

The Company will recognize interest and penalties related to uncertain tax positions in income tax expense. As of December 31, 2016, 2015 and 2014, the Company had no accrued uncertain tax positions or associated interest or penalties and no amounts have been recognized in the Company’s consolidated statements of operations.

The Company files income tax returns in the U.S. federal jurisdiction, and various state jurisdictions. Generally, the Company’s 2013 through 2015 tax years remain open and subject to examination by federal and state taxing authorities. However, federal and state net operating losses from 2009 through 2015 are subject to review by taxing authorities in the year utilized.

8. Commitments and Contingencies

The Company leases approximately 45,362 square feet of office and lab space in Cambridge, Massachusetts under a lease which was most recently amended in July 2016, collectively, the Lease. Total monthly lease payments for base rent are approximately $242,000 per month which is subject to annual rent escalations. In addition to such annual rent escalations, base rent payments for a portion of said premises are scheduled to commence on or about January 1, 2017 in the monthly amount of approximately $22,000. Landlord contributions included in the Lease from the landlord totaled $2,169,920, including $256,765 in leasehold improvements not yet utilized. The landlord contributions are being accounted for as a deferred lease incentive and reduction in monthly rent expense over the term of the Lease. The term of the Lease with respect to the office space expires on September 11, 2026, with one five year extension option available. The term of the Lease for the lab space is five years, with an extension option for one additional period of two years. The total security deposit in connection with the Lease of $1,280,857 is included in other assets in the Company’s condensed consolidated balance sheets as of December 31, 2016 and December 31, 2015.

The Company recognizes rent expense for the space which it currently occupies and records a deferred lease obligation representing the cumulative difference between actual facility lease payments and lease expense recognized ratably over the lease period, which is included in the Company's condensed consolidated balance sheets as of December 31, 2016 and December 31, 2015. The Company will begin recognizing rent expense for the lab space and the remaining office space subsequent to taking possession of the space.

Under the Lease, the Company took possession of the remaining 3,384 square feet of office space on January 1, 2017, and subleased this space commencing on that date (the Sublease) as it did not intend to use the space for its operations. The term of the Sublease is two years and the monthly rent to be received by the Company is approximately $22,000. Under the Sublease, the Company's operating lease obligations through 2018 are partially offset by future Sublease payments to it of approximately $0.5 million. The total security deposit in connection with the Sublease of $21,432 which is due within 30 days from the execution of the Sublease, is included in other current assets and other liabilities in the Company's consolidated balance sheets.

The Company leases office equipment under three year capital leases with payments commencing in February 2014, April 2015 and February 2016, respectively. The capital lease amounts are included in accrued expenses and other liabilities.

At December 31, 2016, the Company's future minimum payments required under these leases are as follows:

	Operating Lease	Lease Payments to be Received from Sublease	Net Operating Lease Payments	Capital Lease	Total
	(in thousands)				
2017	$3,545	$ 257	$ 3,288	$ 9	$3,297
2018	3,545	257	$ 3,288	5	$3,293
2019	3,545	—	$ 3,545	—	$3,545
2020	3,545	—	$ 3,545	—	$3,545
2021	3,510	—	$ 3,510	—	$3,510
Thereafter	14,666	—	$ 14,666	—	$14,666
Total	$32,356	$ 514	$ 31,842	14	$31,856
Less amount representing interest				—	
Present value of minimum lease payments at December 31, 2016				$ 14	

The Company recorded approximately $2.5 million and $0.9 million in rent expense for the years ended December 31, 2016 and 2015, respectively.

Under the Company's agreement with a subsidiary of Quintiles IMS Holdings, Inc., or Quintiles, to provide services for the PRO_2TECT and $INNO_2$VATE programs, the total remaining contract costs as of December 31, 2016 were approximately $406.4 million. The estimated period of performance for the committed work with Quintiles is through the fourth quarter of 2019. The Company contracts with various other organizations to conduct research and development activities with remaining contract costs to the Company of approximately $24.9 million at December 31, 2016. The scope of the services under these research and development contracts can be modified and the contracts cancelled by the Company upon written notice. In some instances, the contracts may be cancelled by the third party upon written notice.

In September 2015, a purported securities class action lawsuit was filed against the Company, including its Chief Executive Officer, its Chief Financial Officer, and members of the Company's Board of Directors, in the Business Litigation Section of the Suffolk County Superior Court of Massachusetts. The complaint is brought on behalf of an alleged class of those who purchased common stock of the Company pursuant or traceable to the Company's initial public offering, and purports to allege claims arising under Sections 11, 12(a)(2) and 15 of the Securities Act of 1933, as amended. The complaint generally alleges that the defendants violated the federal securities laws by, among other things, making material misstatements or omissions concerning the Phase 2b clinical study of vadadustat. The complaint seeks, among other relief, unspecified compensatory damages, rescission of certain stock purchases, attorneys' fees, and costs. In October 2015, the Company removed the case to the United States District Court for the District of Massachusetts, and the plaintiff filed a motion to remand the case back to the Business Litigation Section of the Suffolk County Superior Court of Massachusetts. The plaintiff's motion to remand was granted in April 2016. The plaintiff filed an amended complaint in the Suffolk County Superior Court on August 15, 2016, and the Company served a memorandum in support of its motion to dismiss the amended complaint on October 14, 2016. The motion to

dismiss hearing was held on January 31, 2017. The Court granted the Company's motion to dismiss and dismissed the case with prejudice on February 21, 2017. The plaintiff has 30 days to appeal the decision. The Company believes such claims are without merit and will engage in a vigorous defense of such appeal, if it is ultimately filed by the plaintiff.

The Company has had a number of positive developments in our opposition and invalidity proceedings against FibroGen, Inc., or FibroGen. With regard to the opposition that the Company filed in Europe against FibroGen's European Patent No. 1463823, or the '823 patent, an oral proceeding took place March 8 and 9, 2016. Following the oral proceeding, the European Opposition Division ruled that the patent as granted did not meet the requirements for patentability under the European Patent Convention and, therefore, revoked the patent in its entirety. FibroGen has appealed that decision. Likewise, with regard to the invalidity proceeding that the Company filed in Japan against certain claims of FibroGen's Japanese Patent No. 4804131, or the '131 patent, which is the Japanese counterpart to the '823 patent, the Japan Patent Office, or JPO, issued a preliminary decision finding all of the challenged claims to be invalid. FibroGen subsequently amended the claims and the JPO accepted the amendments. The resulting FibroGen Japanese '131 patent does not cover vadadustat or any pyridine carboxamide compounds. To date, FibroGen has been unsuccessful in its attempts to obtain a patent in the United States covering the same claim scope as it obtained initially in Europe and Japan in the '823 and '131 patents. In the event FibroGen were to obtain such a patent in the United States, the Company may decide to challenge them like the Company has done in Europe and Japan.

On May 13, 2015, May 20, 2015 and July 6, 2015 the Company filed oppositions to FibroGen's European Patent Nos. 2322153, 2322155, and 1633333, or the '153 patent, the '155 patent, and the '333 patent, respectively, requesting the patents be revoked in their entirety. These related patents claim, among other things, various compounds that either stabilize HIF or inhibit a HIF hydroxylase or a HIF prolyl hydroxylase for treating or preventing various conditions, including, inter alia, iron deficiency, microcytosis associated with iron deficiency, anemia of chronic disease, anemia wherein the subject has a transferrin saturation of less than 20%, anemia refractory to treatment with exogenously administered erythropoietin, or EPO, and microcytosis in microcytic anemia. Such method of use patents do not prevent persons from using the compound for other uses, including any previously known use of the compound. In particular, these patents do not claim methods of using any of our product candidates for purposes of inhibiting hypoxia-inducible factor prolyl hydroxylases, or HIF-PHs, for the treatment of anemia secondary to CKD. While we do not believe these patents will prevent us from commercializing vadadustat for treatment of anemia secondary to CKD, we filed these oppositions to provide us and any future partners with maximum flexibility for developing vadadustat and our pipeline of HIF PH inhibitors. With regard to the opposition that we filed in Europe against FibroGen's European Patent No. 163333, or the '333 patent, an oral proceeding took place December 8 and 9, 2016. Following the oral proceeding, the European Opposition Division ruled that the patent as granted did not meet the requirements for patentability under the European Patent Convention and, therefore, revoked the patent in its entirety. FibroGen has appealed that decision. Oppositions to the '155 patent and to the '153 patent were also filed by Glaxo Group Limited, or Glaxo and by Bayer Intellectual Property GmbH, Bayer Pharma Aktiengesellschaft, and Bayer Animal Health GmbH. While, for the reasons set forth in our oppositions, the Company believes that the '153 patent and the '155 patent should be revoked in their entirety, the ultimate outcomes of the oppositions remains uncertain. If the European Patent Office decides not to revoke the '153 patent or the '155 patent in their entirety, or only certain claims of those patents, and any surviving claims are determined to encompass the Company's intended use of the Company's lead product candidate, the Company may not be able to commercialize the Company's lead product candidate in the European Union for its intended use, which could materially adversely affect the Company's business, operating results and financial condition.

The Company's policy is to record a liability if a loss in a significant legal dispute is considered probable and an amount can be reasonably estimated. The Company provides disclosure when a loss in excess of any reserve is reasonably possible, and the Company is in a position to estimate the potential loss or range of possible loss. Significant judgment is required to assess the likelihood of various potential outcomes and the quantification of loss in those scenarios. The Company's estimates change as litigation progresses and new information comes to light. Changes in Company estimates could have a material impact on the Company's results and financial position.

9. Significant Agreements

Mitsubishi Tanabe Pharma Corporation Collaboration Agreement

Summary of Agreement

On December 11, 2015, the Company and MTPC, entered into a collaboration agreement, the MTPC Agreement, providing MTPC with exclusive development and commercialization rights to vadadustat, the Company's product candidate for the treatment of anemia related to chronic kidney disease, in Japan and certain other Asian countries, collectively, the Territory.

Pursuant to the MTPC Agreement, MTPC has an exclusive license to develop and commercialize vadadustat in the Territory. In addition, the Company will supply vadadustat for both clinical and commercial use in the Territory. The countries included in the Territory are Japan, Taiwan, South Korea, Singapore, Malaysia, India, Indonesia, East

Timor, Mongolia, the Philippines, Vietnam, Laos, Cambodia, Thailand, Brunei, Myanmar, Nepal, Sri Lanka, Bangladesh, Bhutan, Maldives, Palau and Tonga and their territories.

In consideration for the exclusive license and other rights contained in the MTPC Agreement, MTPC will make payments totaling up to $350.0 million to fund the vadadustat Phase 3 program (Phase 3 Program), including up to $100.0 million in upfront and development payments, of which $40.0 million was received in January 2016. To the extent Japanese patients are included in the Phase 3 Program, MTPC will fund up to an additional $60.0 million of development costs (Global Scenario). If Japanese patients are not included in the Phase 3 Program (Local Scenario), MTPC will be responsible for the costs of the local Phase 3 study in Japan and make no additional funding payments for the Phase 3 Program. In addition, $20.0 million of the $40.0 million received in 2016 would be used to fund local development of vadadustat in Japan or be refunded to MTPC, at MTPC’s discretion.

The final determination of whether Japanese patients can be included in the Phase 3 Program will be made by the Company and MTPC, in consultation with the Pharmaceuticals and Medical Devices Agency, PMDA, following the results of our Phase 2 studies being conducted in Japan, which is expected in the second half of 2017, unless the Company and MTPC otherwise collectively decide, as provided in the MTPC Agreement, to pursue the Local Scenario prior to such determination by the PMDA.

The Company is also eligible to receive up to approximately $250.0 million in additional payments based upon achievement of certain development, regulatory and sales milestones, as well as tiered double-digit royalty payments on sales of vadadustat in the Territory.

The Company has evaluated all of the development, regulatory and sales milestones that may be received in connection with the MTPC Agreement. In evaluating if a milestone is substantive, the Company assesses whether: (i) the consideration is commensurate with either the Company's performance to achieve the milestone or the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from the Company's performance to achieve the milestone, (ii) the consideration relates solely to past performance, and (iii) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. All development and regulatory milestones are considered substantive on the basis of the contingent nature of the milestone, specifically reviewing factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the milestone as well as the level of effort and investment required. Accordingly, such amounts will be recognized as revenue in full in the period in which the associated milestone is achieved, assuming all other revenue recognition criteria are met. The total aggregate amount of development milestones is $10.0 million and the total aggregate amount of approval milestones is up to $65.0 million. All sales milestones, up to $175.0 million, will be accounted for in the same manner as royalties and recorded as revenue upon achievement of the milestone, assuming all other revenue recognition criteria are met.

The Company will recognize royalty revenue in the period of sale of the related product(s), based on the underlying contract terms, provided that the reported sales are reliably measurable and the Company has no remaining performance obligations, assuming all other revenue recognition criteria are met.

The Company and MTPC have established a joint steering committee to oversee development and commercialization of vadadustat in the Territory, including approval of any development or commercialization plans. Unless earlier terminated, the MTPC Agreement will continue in effect on a country-by-country basis until the later of: expiration of the last-to-expire patent covering vadadustat in such country in the Territory; expiration of marketing or regulatory exclusivity in such country in the Territory; or ten years after the first commercial sale of vadadustat in such country in the Territory. MTPC may terminate the MTPC Agreement upon twelve months' notice at any time after the second anniversary of the effective date of the MTPC Agreement. Either party may terminate the MTPC Agreement upon the material breach of the other party that is not cured within a specified time period or upon the insolvency of the other party.

As of December 31, 2016, the Company cannot determine all of its deliverables or the total amount of consideration to be received for which revenue will be recognized until it knows whether vadadustat will be developed for the Japan market under a Global Scenario or under a Local Scenario. Given the uncertainty around both deliverables and the total consideration to be received, we concluded that we lack sufficient persuasive evidence of an arrangement until these uncertainties are resolved (that is, there is uncertainty regarding our rights and obligations under the arrangement). Under a Global Scenario, our deliverable will be a Services Deliverable as we will be required to include Japanese subjects in our ongoing global Phase 3 study. Under a Local Scenario, our deliverable will be a Supply Deliverable as we will not include Japanese subjects in our ongoing Phase 3 program, but will instead provide clinical supply of vadadustat to MTPC in order for MTPC to conduct a local study. The final determination will be made by the Company and MTPC in consultation with the PMDA following the results of our Phase 2 studies being conducted in Japan, unless the Company and MTPC otherwise decide to pursue the Local Scenario prior to such consultation with the PMDA. Revenue recognition for the MTPC Agreement will commence when all criteria as required under ASC 605 have been satisfied, which the Company expects will be in the second half of 2017. Therefore, the $40.0 million payment received in January 2016 is recorded as deferred revenue in the accompanying consolidated balance sheet.

Otsuka Pharmaceutical Company. Ltd. Collaboration and License Agreement

Summary of Agreement

On December 18, 2016, the Company entered into a collaboration and license agreement with Otsuka, or the Otsuka Agreement. The collaboration is focused on the development and commercialization of vadadustat in the United States. Under the terms of the Otsuka Agreement, the Company will continue to lead the development of vadadustat, including the ongoing Phase 3 development program. The Company and Otsuka will co-commercialize vadadustat in the United States, subject to the approval of vadadustat by the FDA.

Under the terms of the Otsuka Agreement, the Company granted to Otsuka a co-exclusive, non-sublicensable license under certain intellectual property controlled by the Company solely to perform medical affairs activities and to conduct non-promotional and commercialization activities related to vadadustat in accordance with the associated plans. The co-exclusive license relates to activities that will be jointly conducted by the Company and Otsuka pursuant to the terms of the Otsuka Agreement.

Pursuant to the terms of the Otsuka Agreement, the Company is responsible for performing all activities related to the development of vadadustat as outlined in the current global development plan. The current global development plan encompasses all activities that are necessary through the filing of an NDA, including the ongoing PRO_2TECT program and the ongoing $INNO_2VATE$ program, as well as other derivative and ancillary studies. Under the Otsuka Agreement, the Company controls and retains final decision making

authority with respect to the development of vadadustat. The Company's obligations related to the conduct of the current global development plan include the associated manufacturing and supply services for vadadustat.

Under the Otsuka Agreement, the parties will jointly conduct, and will have equal responsibility for, all medical affairs, commercialization and non-promotional activities pursuant to underlying plans as agreed to by the parties. The Company will retain control over and responsibility for the manufacturing and supply of vadadustat during development. If approved by the FDA the Company will provide vadadustat to Otsuka for commercialization pursuant to a separate supply agreement to be negotiated.

The activities under the Otsuka Agreement will be governed by a joint steering committee (JSC) formed by an equal number of representatives from the Company and Otsuka. The JSC will coordinate and monitor the parties' activities under the collaboration. Among other responsibilities, the JSC will manage the overall strategic alignment between the parties, oversee the current global development plan and review the other detailed plans setting forth the parties' activities under the arrangement, including the medical affairs plan and commercialization and non-promotional activities plan. Additionally, the parties will establish a joint development committee (JDC) which will be comprised of an equal number of representatives from the Company and Otsuka. Among other responsibilities, the JDC will share information related to, and review and discuss activities and progress under, the current global development plan and any other development that may be conducted pursuant to the collaboration. In support of the potential commercialization of vadadustat, the parties will establish a joint commercialization committee (JCC) which will be comprised of an equal number of representatives from the Company and Otsuka. Among other responsibilities, the JCC will manage the activities and progress under the commercialization and non-promotional activities plan and all other sales and marketing activities. The Company has retained the final decision making authority with respect to all development matters, pricing strategy and certain other key commercialization matters.

Under the terms of the Otsuka Agreement, the Company received a $125.0 million up-front, non-refundable, non-creditable cash payment in December 2016. In March 2017, the Company received a payment of approximately $33.8 million which represents reimbursement for Otsuka's share of costs previously incurred by the Company in implementing the current global development plan through December 31, 2016. Going forward, Otsuka will contribute a percentage of the remaining costs to be incurred under the current global development plan subsequent to December 31, 2016, commencing upon the date on which the Company has incurred a specified amount of incremental costs. The Company estimates that Otsuka's funding of the current global development plan costs subsequent to December 31, 2016 will total $106.2 million or more. The costs associated with the performance of any development activities in addition to those outlined in the current global development plan will be subject to a cost sharing or reimbursement mechanism to be determined by the parties. Costs incurred with respect to medical affairs and commercialization and non-promotional activities will generally be shared equally by the parties. Either party's share of the medical affairs and/or commercialization activities may be increased at such party's request upon mutual agreement of the parties. In addition, if the costs incurred in completing the activities under the current global development plan exceed a certain threshold, then the Company may elect to require Otsuka to fund a higher percentage of the current global development costs. In such event, the excess of the payments made under such election and Otsuka's allocated share of the current global development costs is fully creditable against future payments due to the Company under the arrangement.

In addition, Otsuka would be required to make certain milestone payments to the Company upon the achievement of specified development, regulatory and commercial events. More specifically, the Company is eligible to receive up to $125.0 million in development milestone payments and up to $65.0 million in regulatory milestone payments for the first product to achieve the associated event. Moreover, the Company is eligible for up to $575.0 million in commercial milestone payments associated with aggregate sales of all products. Due to the uncertainty of pharmaceutical development and the high historical failure rates associated with drug development, no milestone payments may ever be received from Otsuka.

Under the Otsuka Agreement, the Company and Otsuka share the costs of developing and commercializing vadadustat in the United States and the profits from the sales of vadadustat after approval by the FDA. In connection with the profit share calculation, net sales include gross sales to third-party customers net of discounts, rebates, chargebacks, taxes, freight and insurance charges and other applicable deductions. Shared costs generally include costs attributable or reasonably allocable to the manufacture of vadadustat for commercialization purposes and the performance of medical affairs activities, non-promotional activities and commercialization activities.

Under the Otsuka Agreement, Otsuka has a limited period of time in which it can exercise an option to convert the arrangement from a profit share to a right to receive a mid-single digit royalty on future net sales of commercialized products (the Royalty Conversion Option). Upon Otsuka's exercise of the Royalty Conversion Option, the licenses granted to Otsuka will terminate and the parties will cease joint participation in the collaboration. Effective immediately upon the exercise of the Royalty Conversion Option, the Company will be solely responsible for all future development, manufacturing, medical affairs and commercialization and non-promotional activities. Royalties that would be payable to Otsuka upon the exercise of the Royalty Conversion Option are subject to reduction upon the date on which vadadustat ceases to have exclusivity. Royalties would be due on a product-by-product and country-by-

country basis from the date of the first commercial sale of vadadustat in such country until the fifth anniversary of the date on which the licensed product ceases to have exclusivity.

Unless earlier terminated, the Agreement will expire on a country-by-country and product-by-product basis on the date that one or more generic versions of vadadustat first achieves 90% market penetration. Either party may terminate the Otsuka Agreement in its entirety if the other party has materially breached its obligations under the agreement and, after receiving written notice identifying such material breach in reasonable detail, the breaching party fails to cure such material breach. Otsuka may terminate the Otsuka Agreement in its entirety upon 12 months' prior written notice at any time after the release of the first topline data from the global Phase 3 development program. If Otsuka exercises the Royalty Conversion Option and the Company subsequently exercises its right to buy-back the royalty obligation, then the Otsuka Agreement will automatically terminate in its entirety. In the event of termination of the Otsuka Agreement, all rights and licensees granted to Otsuka under the Otsuka Agreement will automatically terminate and the licenses granted to the Company will become freely sublicensable, but potentially subject to a future royalty. In addition, the upfront payment, all development costs and milestone payments received by the Company prior to such termination will not be eligible for reimbursement to Otsuka.

Accounting Analysis

The Company determined that the medical affairs and commercialization and non-promotional activities elements of the License Agreement represent joint operating activities in which both parties are active participants and of which both parties are exposed to significant risks and rewards that are dependent on the commercial success of the activities. Accordingly, the Company is accounting for the joint medical affairs and commercialization and non-promotional activities in accordance with ASC No. 808, Collaborative Arrangements (ASC 808). Additionally, the medical affairs and commercialization and non-promotional activities were not deemed to be deliverables under ASC No. 605-25, Revenue Recognition–Multiple-Element Arrangements (ASC 605-25). As a result, the activities conducted pursuant to the medical affairs and commercialization and non-promotional activities plans will be accounted for as a component of the related expense in the period incurred. The Company evaluated the other elements of the License Agreement in accordance with the provisions of ASC 605-25. The Company's arrangement with Otsuka contains the following deliverables: (i) license under certain of the Company's intellectual property to develop, perform medical affairs activities with respect to and conduct non-promotional and commercialization activities related to vadadustat and products containing or comprising vadadustat (the License Deliverable), (ii) development services to be performed pursuant to the current global development plan (the R&D Development Services Deliverable), (iii) rights to future intellectual property and (iv) joint committee services.

Factors considered in making the assessment of standalone value included, among other things, the capabilities of the collaboration partner, whether any other vendor sells the item separately, whether the value of the deliverable is dependent on the other elements in the arrangement, whether there are other vendors that can provide the items and if the customer could use the item for its intended purpose without the other deliverables in the arrangement. Additionally, the License Agreement does not include a general right of return. Accordingly, each of the other deliverables included in the Otsuka arrangement qualifies as a separate unit of accounting. Therefore, the Company has identified the following three units of accounting in connection with its obligations under the collaboration arrangement with Otsuka as follows:

(i) License and R&D Development Services Combined

The License Deliverable does not have standalone value separate from the R&D Development Services Deliverable, due to the contractual limitations inherent in the license conveyed. More specifically, Otsuka does not have the contractual right to manufacture vadadustat and products containing or comprising vadadustat. However, the manufacturing and supply services that are conducted as part of the services to be performed pursuant to the current global development plan are necessary for Otsuka to fully exploit the associated license for its intended purpose. The value of the rights provided through the license conveyed will be realized when the underlying products covered by the intellectual property progress through the development cycle, receive regulatory approval and are commercialized. Products containing or comprising vadadustat cannot be commercialized until the development services under the current global development plan are completed. Accordingly, Otsuka must obtain the manufacturing and supply of the associated products that is included within the development services to be performed pursuant to the current global development plan from the Company in order to derive benefit from the license which significantly limits the ability for Otsuka to utilize the License Deliverable for its intended purpose on a standalone basis.

(ii)Rights to Future Intellectual Property

The License Deliverable and the R&D Development Services deliverable have standalone value from the Rights to Future Intellectual Property because Otsuka can obtain the value of the license using the clinical trial materials implicit in the

development services without the receipt of any other intellectual property that may be discovered or developed in the future.

(iii)Joint Committee Services

The Joint Committee Services has standalone value from the License and R&D Services deliverables because Otsuka can obtain the value of the license using the clinical trial materials implicit in the development services without the joint committee services. The Joint Committee Services has standalone value from the Rights to Future Intellectual Property because the Joint Committee Services have no bearing on the value to be derived from the rights to potential future intellectual property.

The Company has determined that neither VSOE of selling price nor TPE of selling price is available for any of the units of accounting identified at inception of the arrangement with Otsuka. Accordingly, the selling price of each unit of accounting was determined based on the Company's BESP. The Company developed the BESP with the objective of determining the price at which it would sell such an item if it were to be sold regularly on a standalone basis. In developing the BESP for the Joint Committee Services Unit of Accounting, the Company considered the nature of the services to be performed and estimates of the associated effort and rates applicable to such services that would be expected to be realized under similar contracts. The Company developed the BESP for the Rights to Future Intellectual Property Unit of Accounting primarily based on the likelihood that additional intellectual property covered by the license conveyed will be developed during the term of the arrangement. The Company did not develop a BESP for the License Unit of Accounting due to the following: (i) the BESP associated with the Rights to Future Intellectual Property Unit of Accounting was determined to be immaterial and (ii) the period of performance and pattern of recognition for the License Unit of Accounting and the Joint Committee Services Unit of Accounting was determined to be similar. The Company has concluded that a change in the key assumptions used to determine the BESP for each unit of accounting would not have a significant impact on the allocation of arrangement consideration.

Allocable arrangement consideration at inception is comprised of: (i) the up-front payment of $125.0 million, (ii) the cost share payment with respect to amounts incurred by the Company through December 31, 2016 of $33.8 million and (iii) an estimate of the cost share payments to be received with respect to amounts incurred by the Company subsequent to December 31, 2016 of $106.2 million. The cost share payments to be received represent contingent revenue features because the Company's retention of the associated arrangement consideration is dependent upon its future performance of development services. No amounts were allocated to the Rights to Future Intellectual property Unit of Accounting because the associated BESP was determined to be immaterial. Due to the similar performance period and recognition pattern between the License Unit of Accounting and the Joint Committee Services Unit of Accounting, the arrangement consideration totaling $265.0 million has been allocated to the License Unit of Accounting and the Joint Committee Services Unit of Accounting on a combined basis. Accordingly, the Company will recognize revenue related to the allocable arrangement consideration on a proportional performance basis as the underlying development services are performed pursuant to the current global development plan which is commensurate with the period and consistent with the pattern over which the Company's obligations are satisfied for both the License Unit of Accounting and the Joint Committee Services Unit of Accounting. Effectively, the Company has treated the arrangement as if the License Unit of Accounting and the Joint Committee Services Unit of

Accounting are a single unit of accounting.

The Company has evaluated all of the development, regulatory and commercial milestones that may be received in connection with the License Agreement. In evaluating if a milestone is substantive, the Company assesses whether: (i) the consideration is commensurate with either the Company's performance to achieve the milestone or the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from the Company's performance to achieve the milestone, (ii) the consideration relates solely to past performance, and (iii) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. All development and regulatory milestones are considered substantive on the basis of the contingent nature of the milestone, specifically reviewing factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the milestone as well as the level of effort and investment required. Accordingly, such amounts will be recognized as revenue in full in the period in which the associated milestone is achieved, assuming all other revenue recognition criteria are met. All commercial milestones will recorded as revenue upon achievement of the milestone, assuming all other revenue recognition criteria are met.

The Company will recognize royalty revenue in the period of sale of the related product(s), based on the underlying contract terms, provided that the reported sales are reliably measurable and the Company has no remaining performance obligations, assuming all other revenue recognition criteria are met.

During the year ended December 31, 2016, the Company recognized revenue totaling approximately $1.5 million with respect to the License Agreement. The revenue is classified as collaboration revenue in the accompanying consolidated statement of operations. As of December 31, 2016, there is approximately $157.3 million of deferred revenue related to the License Agreement which is classified as

current or long-term in the accompanying consolidated balance sheet based on the performance period of the underlying obligations. During the year ended December 31, 2016, the Company did not incur any costs related to the cost-sharing provisions of the License Agreement. In addition, as of December 31, 2016, the Company recorded a $33.8 million unbilled receivable related to the reimbursable development costs under the License Agreement for activities performed through December 31, 2016. The Company received payment of the $33.8 million in March 2017.

10. Employee Retirement Plan

During 2008, the Company established a retirement plan (the Plan) authorized by Section 401(k) of the Internal Revenue Code. In accordance with the Plan, all employees who have attained the age of 21 are eligible to participate in the Plan as of the first Entry Date, as defined, following their date of employment. Each employee can contribute a percentage of compensation up to a maximum of the statutory limits per year. Company contributions are discretionary and contributions in the amount of approximately $0.2 million, $0.1 million and $0 were made during the year ended December 31, 2016, 2015 and 2014, respectively.

11. Net Loss per Share

The following table presents the calculation of basic and diluted net loss per share applicable to common stockholders:

	Year ended December 31,		
	2016	2015	2014
	(in thousands, except share and per share data)		
Numerator:			
Net loss	$(135,747)	$(60,716)	$(37,034)
Accretion on preferred stock	—	—	(86,899)
Net loss applicable to common stockholders	$(135,747)	$(60,716)	$(123,933)
Denominator:			
Weighted-average number of common shares – basic and diluted	37,716,949	26,469,170	15,406,386
Net loss per share applicable to common stockholders – basic and diluted	$(3.60)	$(2.29)	$(8.04)

The shares in the table below were excluded from the calculation of diluted net loss per share, prior to the use of the treasury stock method, due to their anti-dilutive effect:

	Year ended December 31,		
	2016	2015	2014
Outstanding stock options	3,148,006	2,206,635	1,526,346
Unvested restricted stock	92,972	216,716	422,145
Unvested restricted stock units	431,688	24,425	—
Total	3,672,666	2,447,776	1,948,491

12. Quarterly Results (unaudited)

	Three Months Ended March 31, 2016	June 30, 2016	September 30, 2016	December 31, 2016
	(in thousands, except per share data) (unaudited)			
Collaboration revenue	$—	$—	$ —	$ 1,535
Operating expenses	$26,046	$36,188	$ 36,182	$ 39,579
Loss from operations	$(26,046)	$(36,188)	$ (36,182)	$ (38,044)
Other income (expense), net	$248	$409	$ (126)	$ 182
Net loss	$(25,798)	$(35,779)	$ (36,308)	$ (37,862)
Net loss per share applicable to common stockholders—basic and diluted	$(0.70)	$(0.95)	$ (0.96)	$ (0.99)

	Three Months Ended March 31, 2015	June 30, 2015	September 30, 2015	December 31, 2015
	(in thousands, except per share data) (unaudited)			
Collaboration revenue	$—	$—	$ —	$ —
Operating expenses	$10,896	$10,889	$ 19,678	$ 20,050
Loss from operations	$(10,896)	$(10,889)	$ (19,678)	$ (20,050)
Other income (expense), net	$201	$200	$ 203	$ 193
Net loss	$(10,695)	$(10,689)	$ (19,475)	$ (19,857)
Net loss per share applicable to common stockholders—basic and diluted	$(0.53)	$(0.40)	$ (0.68)	$ (0.66)

13. Subsequent Event

In February 2017, the Company entered into a Research and License Agreement, the Agreement, with Janssen Pharmaceutica NV, one of the Janssen Pharmaceutical Companies of Johnson and Johnson, Janssen, pursuant to which Janssen granted the Company an exclusive license under certain intellectual property rights to develop and commercialize worldwide certain HIF-PH targeted compounds, as well as develop and commercialize JNJ5169, a preclinical compound in development as an oral treatment for IBD.

Under the terms of the Agreement, the Company will pay an upfront payment of $1.0 million to Janssen within 30 days of execution of the Agreement. In addition, Janssen could be eligible to receive up to an aggregate of $16.5 million from the Company in specified development milestone payments on a product-by-product basis. Janssen will also be eligible to receive up to $215.0 million from the Company in specified commercial milestones as well as tiered, escalating royalties ranging from a low to mid-single digit percentage of net sales, on a product-by-product basis.

In connection with its entry into the Agreement, in February, 2017, the Company issued a Common Stock Purchase Warrant, the Warrant, to Johnson & Johnson Innovation – JJDC, Inc., or JJDC, an affiliate of Janssen, for 509,611 shares of the Company's common stock at an exercise price of $9.81 per share. The Warrant is exercisable by JJDC, in whole or in part, at any time prior to the fifth anniversary of the date of issuance. The Warrants and the shares issuable upon exercise of the Warrants will be sold and issued without registration under the Securities Act of 1933, the Securities Act.

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

None.

Item 9A. Controls and Procedures
Controls and Procedures

Management's Annual Report on Internal Control over Financial Reporting

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) under 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. Management conducted an assessment of the effectiveness of our internal control over financial reporting based on the criteria set forth in Internal Control - Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework). Based on the assessment, management has concluded that its internal control over financial reporting was effective as of December 31, 2016 to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with U.S. GAAP.

Management's Evaluation of our Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Securities Exchange Act of 1934 is (1) recorded, processed, summarized, and reported within the time periods specified in the SEC's rules and forms and (2) accumulated and communicated to our management, including our principal executive officer and principal financial officer, to allow timely decisions regarding required disclosure.

As of December 31, 2016, our management, with the participation of our principal executive officer and principal financial officer, evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934). Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives, and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Our principal executive officer and principal financial officer have concluded based upon the evaluation described above that, as of December 31, 2016, our disclosure controls and procedures were effective at the reasonable assurance level.

Changes in Internal Control over Financial Reporting

During the quarter ended December 31, 2016, there have been no changes in our internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15(d)-15(f) promulgated under the Securities Exchange Act of 1934, that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information
Other Information

The following disclosure is provided in accordance with and in satisfaction of the requirements of Item 2.02 “Results of Operations and Financial Condition” of Form 8-K:

On March 6, 2017, Akebia announced its financial results for the quarter ended December 31, 2016 and commented on certain corporate accomplishments and plans. The full text of the press release issued in connection with the announcement is furnished as Exhibit 99.1 hereto.

The information furnished in Item 9B (including Exhibit 99.1) shall not be deemed “filed” for purposes of Section 18 of the Exchange Act, or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such a filing.

PART III

Certain information required by Part III is omitted from this Annual Report on Form 10-K and is incorporated herein by reference from our definitive proxy statement relating to our 2017 Annual Meeting of Stockholders (the "Definitive Proxy Statement"), which we expect to file with the SEC no later than April 30, 2017.

Item 10. Director, Executive Officers and Corporate Governance

John P. Butler joined Akebia as director in July 2013 and was appointed as the President and Chief Executive Officer of Akebia in August 2013. Prior to joining Akebia, from 2011 until 2013, Mr. Butler served as the Chief Executive Officer of Inspiration Biopharmaceuticals, Inc., a company focused on developing products for patients with hemophilia. Mr. Butler led the transactions that resulted in the sale of hemophilia assets to Cangene Corporation and Baxter International in early 2013 for total aggregate consideration that could exceed $1 billion. From 1997 to 2011, Mr. Butler held various positions at Genzyme Corporation, a biopharmaceutical company, most recently serving as President of the company's rare genetic diseases business. From 2002 until 2010, Mr. Butler led Genzyme's renal division. Prior to his work at Genzyme, Mr. Butler held sales and marketing positions at Amgen and Hoffmann-La Roche. Mr. Butler currently serves as a member of the Board of Trustees for the American Kidney Fund and Chairman of the Board of Directors of Keryx Biopharmaceuticals, Inc. Mr. Butler received a B.A. in Chemistry from Manhattan College and an M.B.A. degree from Baruch College, City University of New York. We believe that Mr. Butler is qualified to serve on our board of directors due to his industry experience in the biotechnology sector, particularly his experience working in the renal disease market.

Jason A. Amello joined Akebia as Senior Vice President, Chief Financial Officer and Treasurer in 2013. Prior to joining Akebia, Mr. Amello served as Executive Vice President, Chief Financial Officer and Treasurer of ZIOPHARM Oncology, Inc., a biopharmaceutical company, from 2012 to 2013. From 2000 to 2011, Mr. Amello held various positions at Genzyme Corporation, most recently as Senior Vice President, Corporate Controller and Chief Accounting Officer, and led the Strategic Financial Services group through which he served as a key advisor on all of Genzyme's M&A and strategic transactions. Earlier in his career, Mr. Amello spent 10 years in the business advisory and assurance practice of Deloitte, serving in various roles of increasing responsibility through senior manager. Mr. Amello currently serves on the Board of Directors of the New England Baptist Hospital and is Chair of the Quality of Care Committee and a member of the Finance and Investment Committee. Mr. Amello holds a B.A. from Boston College and is a Certified Public Accountant in the Commonwealth of Massachusetts.

Brad Maroni, M.D. joined Akebia as Senior Vice President and Chief Medical Officer in August 2014. Dr. Maroni most recently served as Vice President, Medical Research at Biogen Idec. Prior to that role, Dr. Maroni served as Chief Medical Officer of Stromedix, Inc. until the company was acquired by Biogen Idec in 2012. His previous experience also includes serving as Executive Vice President and Chief Medical Officer at RenaMed Biologics, as well as multiple roles at Amgen Inc., including Vice President, Clinical Development and Anemia/Nephrology Therapeutic Area Head. At Amgen, Dr. Maroni led the cross-functional team responsible for the registration program and global regulatory approval of Aranesp®, a novel long-acting recombinant erythropoietic protein, indicated for the treatment of anemia in chronic kidney disease. During his tenure, Amgen also received approval for Sensipar®, a first-in-class small molecule for the treatment of bone disease in dialysis patients. Dr. Maroni trained as a nephrologist at Brigham and Women's Hospital in Boston, Massachusetts, after which he spent 10 years in academia at Emory University.

Nicole R. Hadas joined Akebia in 2013 and is Senior Vice President, General Counsel and Secretary. Prior to joining Akebia, Ms. Hadas was Vice President and General Counsel at OvaScience, Inc., a biopharmaceutical company, in 2013. Ms. Hadas served as the Senior Vice President and General Counsel at Inspiration Biopharmaceuticals, Inc.,

where she managed the successful sale of its hemophilia assets to Cangene Corporation and Baxter International in early 2013. From 2001 to 2011, Ms. Hadas worked at Genzyme Corporation, most recently as Senior Corporate Counsel. Prior to Genzyme, she was an associate at Foley Hoag representing biopharmaceutical companies and healthcare providers in a wide variety of matters. Ms. Hadas received a B.A. from the University of Michigan and a J.D. from Boston College Law School.

Michel Dahan joined Akebia in 2013 and is the Senior Vice President, Chief Business Officer. Prior to joining Akebia, from 2010 to 2013, Mr. Dahan held various positions at Inspiration Biopharmaceuticals, Inc., most recently as Vice President, Commercial Development and Strategic Planning, and led the global marketing and commercial development in preparation for two global launches. Prior to that, from 2003 to 2010, Mr. Dahan served in various roles for Ipsen, most recently as Senior Director, Strategic Planning, working on global marketing and strategic planning for their hemophilia franchise. He began his career at BNP Paribas in 2002 as an analyst on the Business Valuation Team working on mergers and acquisitions and investment banking. He earned his graduate degree in business administration at HEC Paris (France), his maitrise in mathematics from University Paris VI (France), and his executive education program (PLD) at Harvard Business School.

Karen Tubridy joined Akebia as Senior Vice President, Chief Development Officer, in November 2016. Prior to joining Akebia, Ms. Tubridy served as Chief Development Officer of Eleven Biotherapeutics from June 2013 to September 2016. Prior to joining Eleven Biotherapeutics, Ms. Tubridy served as the Senior Vice President, Clinical Development and Medical Affairs of Inspiration Biopharmaceuticals, Inc. from December 2011 to March 2013. Prior to joining Inspiration Biopharmaceuticals, Ms. Tubridy served as the Executive Director, Clinical Operations and Regulatory Affairs, Translational Medicine of Alexion Pharmaceuticals from January 2011 to November 2011, when Taligen Therapeutics was acquired by Alexion Pharmaceuticals, and as Vice President of Clinical Operations and Regulatory Affairs of Taligen Therapeutics from April 2010 to January 2011. Prior to that, Ms. Tubridy served as Vice President of Clinical Operations Hemophilia of Biogen Idec, Inc., a biotechnology company, from January 2007 through March 2010. Ms. Tubridy received a B.S. and a Pharm.D. from the Massachusetts College of Pharmacy and Allied Health Sciences.

The remaining information required by this Item 10 will be contained in the Definitive Proxy Statement and is incorporated herein by reference.

Item 11. Executive Compensation

The information required by this Item 11 will be contained in the Definitive Proxy Statement 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 contained in the Definitive Proxy Statement and is incorporated herein by reference.

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

The information required by this Item 13 will be contained in the Definitive Proxy Statement and is incorporated herein by reference.

Item 14. Principal Accountant Fees and Services

The information required by this Item 14 will be contained in the Definitive Proxy Statement and is incorporated herein by reference.

PART IV

Item 15. Exhibits and Financial Statement Schedules

Exhibits and Financial Statement Schedules

(a) Documents filed as part of Form 10-K.

(1) Financial Statements

Report of Independent Registered Public Accounting Firm

Consolidated Balance Sheets

Consolidated Statements of Operations and Comprehensive Loss

Consolidated Statements of Stockholders' Equity (Deficit)

Consolidated Statements of Cash Flows

Notes to Consolidated Financial Statements

(2) Schedules

Schedules have been omitted as all required information has been disclosed in the financial statements and related footnotes.

(3) Exhibits

The Exhibits listed in the Exhibit Index are filed as a part of this Form 10-K.

Item 16. Form 10-K Summary

Not applicable.

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SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

AKEBIA THERAPEUTICS, INC.

Date: March 6, 2017

By: /s/ John P. Butler
John P. Butler
Chief Executive Officer and President (Principal Executive Officer)

Under the requirements of the Securities and Exchange Act of 1934, this report was signed by the following persons on behalf of the Registrant and in the capacities and on the date indicated.

Date: March 6, 2017

By: /s/ John P. Butler
John P. Butler
Chief Executive Officer and President (Principal Executive Officer)

Date: March 6, 2017

By: /s/ Jason A. Amello
Jason A. Amello
Senior Vice President, Chief Financial Officer and Treasurer (Principal Financial and Accounting Officer)

Date: March 6, 2017

By: /s/ Muneer A. Satter
Muneer A. Satter
Chairman

Date: March 6, 2017

By: /s/ Duane Nash
Duane Nash
Director

Date: March 6, 2017

By: /s/ Michael S. Wyzga
Michael S. Wyzga
Director

By: /s/ Maxine Gowen

Date: March 6, 2017		Maxine Gowen Director
Date: March 6, 2017	By:	/s/ Michael D. Clayman Michael D. Clayman Director
Date: March 6, 2017	By:	/s/ Ronald C. Renaud, Jr. Ronald C. Renaud, Jr. Director
Date: March 6, 2017	By:	/s/ Scott A. Canute Scott A. Canute Director

EXHIBIT INDEX

Exhibit Number	Description of Exhibit
3.1	Ninth Amended and Restated Certificate of Incorporation (incorporated by reference to exhibit 3.1 to the Company's Current Report on Form 8-K, filed on March 28, 2014)
3.2	Amended and Restated Bylaws (incorporated by reference to exhibit 3.2 to the Company's Current Report on Form 8-K, filed on March 28, 2014)
4.1	Form of Common Stock Certificate (incorporated by reference to exhibit 4.1 to the Company's Registration Statement on Form S-1/A (333-193969), filed on March 4, 2014)
4.2	Third Amended and Restated Voting Agreement, dated May 10, 2013 (incorporated by reference to exhibit 4.2 to the Company's Registration Statement on Form S-1 (333-193969), filed on February 14, 2014)
4.3	Amendment No. 1 to the Third Amended and Restated Voting Agreement, dated May 31, 2013 (incorporated by reference to exhibit 4.3 to the Company's Registration Statement on Form S-1 (333-193969), filed on February 14, 2014)
4.4	Fourth Amended and Restated Investors' Rights Agreement, dated March 5, 2014 (incorporated by reference to exhibit 4.4 to the Company's 10-K for the year ending December 31, 2014 and filed on March 4, 2015)
10.1	Form of Director and Officer Indemnification Agreement (incorporated by reference to exhibit 10.1 to the Company's Registration Statement on Form S-1/A (333-193969), filed on March 4, 2014)
10.2	Office Lease Agreement Between MA-Riverview/245 First Street, L.L.C. and Akebia Therapeutics, Inc., dated December 3, 2013 (incorporated by reference to exhibit 10.2 to the Company's Registration Statement on Form S-1 (333-193969), filed on February 14, 2014)
10.3	First Amendment to Office Lease Agreement Between Jamestown Premier 245 First, LLC and Akebia Therapeutics, Inc., dated December 15, 2014 (incorporated by reference to exhibit 10.3 to the Company's 10-K for the year ending December 31, 2014 and filed on March 4, 2015)
10.4	Second Amendment to Office Lease Agreement Between Jamestown Premier 245 First, LLC and Akebia Therapeutics, Inc., dated November 23, 2015 (incorporated by reference to exhibit 10.4 to the Company's 10-K for the year ending December 31, 2015 and filed on March 14, 2016)
10.5	Third Amendment to Office Lease Agreement Between Jamestown Premier 245 First, LLC and Akebia Therapeutics, Inc., dated July 25, 2016 (incorporated by reference to exhibit 10.1 to the Company's Quarterly Report on Form 10-Q, filed on November 9, 2016)
10.6†	Amended and Restated 2008 Equity Incentive Plan (incorporated by reference to exhibit 10.5 to the Company's Registration Statement on Form S-1 (333-193969), filed on February 14, 2014)
10.7†	

	Amendment No. 1 to Amended and Restated 2008 Equity Incentive Plan (incorporated by reference to exhibit 10.6 to the Company's Registration Statement on Form S-1 (333-193969), filed on February 14, 2014)
10.8†	Executive Employment Agreement with John P. Butler, dated September 16, 2013 (incorporated by reference to exhibit 10.7 to the Company's Registration Statement on Form S-1 (333-193969), filed on February 14, 2014)
10.9†	Executive Employment Agreement with Jason A. Amello, dated September 23, 2013 (incorporated by reference to exhibit 10.8 to the Company's Registration Statement on Form S-1 (333-193969), filed on February 14, 2014)
10.10†	Offer Letter to Nicole R. Hadas, dated November 13, 2013 (incorporated by reference to exhibit 10.9 to the Company's Registration Statement on Form S-1 (333-193969), filed on February 14, 2014)
10.11†	Executive Employment Agreement with Dr. Robert Shalwitz, dated April 6, 2011 (incorporated by reference to exhibit 10.10 to the Company's Registration Statement on Form S-1 (333-193969), filed on February 14, 2014)
10.12†	Separation Agreement with Dr. Robert Shalwitz, dated August 5, 2014 (incorporated by reference to exhibit 10.1 to the Company's Quarterly Report on Form 10-Q, filed on November 10, 2014)
10.13†	Consulting Agreement with Dr. Robert Shalwitz, dated August 5, 2014 (incorporated by reference to exhibit 10.2 to the Company's Quarterly Report on Form 10-Q, filed on November 10, 2014)
10.14†	Offer Letter with Bradley Maroni, M.D., dated July 21, 2014 (incorporated by reference to exhibit 10.17 to the Company's 10-K for the year ending December 31, 2014 and filed on March 4, 2015)

Exhibit Number	Description of Exhibit
10.15†	Form of Non-Statutory Stock Option Agreement for officers (incorporated by reference to exhibit 10.24 to the Company's Registration Statement on Form S-1/A (333-193969), filed on March 4, 2014)
10.16†	Form of Non-Statutory Stock Option Agreement for non-employee directors (incorporated by reference to exhibit 10.25 to the Company's Registration Statement on Form S-1/A (333-193969), filed on March 4, 2014)
10.17†	Non-Employee Director Compensation Program (incorporated by reference to exhibit 10.26 to the Company's Registration Statement on Form S-1/A (333-193969), filed on March 4, 2014)
10.18†	Form of Executive Severance Agreement for officers (incorporated by reference to exhibit 10.27 to the Company's Registration Statement on Form S-1/A (333-193969), filed on March 4, 2014)
10.19†	2014 Incentive Plan (incorporated by reference to exhibit 10.29 to the Company's Registration Statement on Form S-1/A (333-193969), filed on March 4, 2014)
10.20†	2014 Employee Stock Purchase Plan (incorporated by reference to exhibit 10.30 to the Company's Registration Statement on Form S-1/A (333-193969), filed on March 4, 2014)
10.21†	Cash Incentive Plan (incorporated by reference to exhibit 10.31 to the Company's Registration Statement on Form S-1/A (333-193969), filed on March 4, 2014)
10.22#	Master Services Agreement by and between Evonik Corporation and Akebia Therapeutics, Inc., dated February 28, 2014 (incorporated by reference to exhibit 10.32 to the Company's Registration Statement on Form S-1/A (333-193969), filed on March 4, 2014)
10.23†	Form of Restricted Stock Unit Award Agreement under 2014 Incentive Plan (incorporated by reference to exhibit 10.26 to the Company's 10-K for the year ending December 31, 2014 and filed on March 4, 2015)
10.24#	Master Services Agreement, between Akebia Therapeutics, Inc., and Quintiles, Inc., dated as of June 8, 2015 (incorporated by reference to exhibit 10.1 to the Company's Quarterly Report on Form 10-Q, filed on August 11, 2015)
10.25#	Collaboration Agreement between Akebia Therapeutics, Inc. and Mitsubishi Tanabe Pharma Corporation, dated December 11, 2015 (incorporated by reference to exhibit 10.29 to the Company's 10-K for the year ending December 31, 2015 and filed on March 14, 2016)
10.26*#	Collaboration and License Agreement, between Akebia Therapeutics, Inc. and Otsuka Pharmaceutical Co. Ltd., dated December 18, 2016
21.1*	List of Subsidiaries
23.1*	Consent of Ernst & Young LLP
31.1*	Certification of Principal Executive Officer Required Under Rule 13a-14(a) of the Securities Exchange Act of 1934, as amended

31.2*	Certification of Principal Financial Officer Required Under Rule 13a-14(a) of the Securities Exchange Act of 1934, as amended
32.1*	Certification of Principal Executive Officer and Principal Financial Officer Required Under Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, and 18 U.S.C. 1350
99.1	Press Release issued by Akebia Therapeutics, Inc. on March 6, 2017 (furnished herewith)
101.INS*	XBRL Instance Document
101.SCH*	XBRL Taxonomy Extension Schema Document
101.CAL*	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	XBRL Taxonomy Extension Labels Linkbase Document
101.PRE*	XBRL Taxonomy Extension Presentation Linkbase Document

* Filed, or submitted electronically, herewith
† Indicates management contract or compensatory plan
# Indicates portions of the exhibit (indicated by asterisks) have been omitted pursuant to a request for confidential treatment
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