Akebia™ THERAPEUTICS

Exploring the Therapeutic Power of Altitude

2017
ANNUAL REPORT

April 2018

Dear Fellow Shareholders,

Those of you who have followed our company over the past several years know the dedication we have put toward developing what we believe has the potential to be a transformative new treatment for patients with anemia due to chronic kidney disease, a serious condition that has seen no meaningful innovation since long-acting injectable erythropoiesis-stimulating agents (ESAs) came to market nearly two decades ago.

So it is with a sense of pride that I report a year of remarkable productivity for our company, and a sense of excitement as I look to the year ahead.

In the past year, we advanced our global Phase 3 clinical program for our lead product candidate, vadadustat, an oral hypoxia-inducible factor prolyl hydroxylase inhibitor (HIF-PHI). We are targeting full enrollment in our PRO$_2$TECT and INNO$_2$VATE registration studies by the end of 2018, with top-line results anticipated in 2019, subject to the accrual of MACE, and market launch planned in 2020, subject to regulatory approval. We revised the designs of our Phase 2 FO$_2$RWARD and Phase 3 TRILO$_2$GY studies, now referred to as FO$_2$RWARD-2 and TRILO$_2$GY-2, which we believe will provide important characterization and differentiation of vadadustat and further strengthen our position in global markets, subject to regulatory approval and commercialization. In addition, our collaboration partner, Mitsubishi Tanabe Pharma Corporation, initiated four Phase 3, non-MACE-dependent studies of vadadustat in Japan, with data read-outs expected in 2019.

We completed significant collaboration and licensing deals to provide us with R&D financing, a stronger commercial presence at launch and significant validation of vadadustat. These efforts include our expanded collaboration with Otsuka for vadadustat, from U.S. only, to include Europe, China and other territories. Otsuka has invested extensively in the cardio-renal area, shares our commitment to bringing important new medicines to patients and has established a strong commercial infrastructure in key markets. This collaboration will provide significant support for the launch of a product with vadadustat's market potential, subject to its regulatory approval. The commitment and insights from our collaboration partners enhance Akebia's strengths.

We also entered into an exclusive license agreement with Vifor Pharma to sell vadadustat as its only HIF-PHI product for distribution to Fresenius in the U.S., a kidney dialysis provider that serves nearly 40 percent of U.S. dialysis patients, subject to FDA approval of vadadustat and inclusion in a bundled reimbursement model. This strategic agreement gives Akebia the opportunity to rapidly build commercial momentum in the U.S. after launch.

Further, we signed an exclusive agreement with Johnson & Johnson Innovation to in-license an extensive library of well-characterized HIF pathway compounds with potential applications across multiple therapeutic areas. We continue to seek business development opportunities to grow our company.

Leveraging our strong momentum, we will focus our efforts to continue to drive progress in our global Phase 3 clinical program. We advance our business from a position of financial strength, with cash resources and significant committed capital from our collaborators that we expect will fund our current operating plan into the first quarter of 2020. Our long-term vision is to grow into a leading innovation-driven commercial renal company. Our achievements would not be possible without our talented and dedicated employees, the patient and medical communities and our shareholders. We appreciate your support.

John P. Butler
President and Chief Executive Officer

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, 2017

OR

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

Commission File Number 001-36352

AKEBIA THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**20-8756903**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
245 First Street, Suite 1100, Cambridge, MA	**02142**
(Address of principal executive offices)	**(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, 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, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer", "accelerated filer", "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

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

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

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the 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 registrant's common stock on The NASDAQ Global Market on June 30, 2017, was $576,393,274.

The number of shares of registrant's common stock outstanding as of March 1, 2018 was 48,346,171.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Proxy Statement for the registrant's 2018 Annual Meeting of Stockholders 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 provisions of the U.S. Private Securities Litigation Reform Act of 1995 with the intention of obtaining the benefits of the "safe harbor" provisions of that Act. These forward-looking statements may be accompanied by words such as "anticipate," "believe," "contemplate," "continue," "could," "designed," "estimate," "expect," "forecast," "future," "goal," "intend," "likely," "may," "plan," "possible," "potential," "predict," "project," "strategy," "seek," "should," "target," "will," "would," and other words and terms of similar meaning. These forward-looking statements include, but are not limited to, statements about:

- the potential therapeutic applications of the HIF pathway;
- the potential of our pipeline and our research activities;
- the potential therapeutic benefits, safety profile, and effectiveness of our product candidates, including the potential for vadadustat to set a new standard of care in the treatment of anemia due to chronic kidney disease
- the potential indications and market potential and acceptance of our product candidates;
- our competitive position, including estimates, developments and projections relating to our competitors and their products and product candidates, and our industry;
- our expectations, projections and estimates regarding our costs, revenues, capital requirements, need for additional capital, cash flows, financial performance, profitability, tax obligations, liquidity, growth, contractual obligations, the period of time our cash resources and collaboration funding will fund our current operating plan, internal control over financial reporting, disclosure controls and procedures;
- the timing of the availability and presentation of clinical trial data and results;
- our and our collaborators' strategy, plans and expectations with respect to the development, manufacturing, commercialization, launch, marketing and sale of our product candidates, and the associated timing thereof;
- the designs of our studies, and the type of information and data expected from our studies;
- the timing of or likelihood of regulatory filings and approvals, including labeling or other restrictions;
- the targeted timing of enrollment of our clinical trials;
- the timing of initiation of our clinical trials and plans to conduct preclinical and clinical studies in the future;
- the timing and amounts of payments from our collaborators and licensees, and the anticipated arrangements and benefits under our collaboration and license agreements;
- our intellectual property position, including obtaining and maintaining patents; and the timing, outcome and impact of administrative, regulatory, legal and other proceedings relating to our patents and other proprietary and intellectual property rights;
- the impact of accounting standards and estimates;
- our facilities, lease commitments, and future availability of facilities;
- our employees, employee compensation, and employee relations; and
- the implementation of our business model and strategic plans for our business, product candidates and technology.

These forward-looking statements involve risks and uncertainties, including those that are described in Part I, Item 1A. Risk Factors included in this Annual Report and elsewhere in this Annual Report, that could cause our actual results, financial condition, performance or achievements to be materially different from those indicated in these forward-looking statements. Given these risks and uncertainties, you should not place undue reliance on these forward-looking statements. Forward-looking statements speak only as of the date of this Annual Report on Form 10-K. Except as required by law, we assume no obligation to publicly update or revise these forward-looking statements for any reason.

This Annual Report on Form 10-K also contains estimates and other information concerning our industry and the markets for certain diseases, including data regarding the estimated size of those markets, and the incidence and prevalence of certain medical conditions. Unless otherwise expressly stated, we obtained this industry, 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 commercializing 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 and has the potential to set a new standard of care in the treatment of anemia due to chronic kidney disease, or 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 potentially address serious diseases.

HIF, a pathway involving hundreds of genes, is the same pathway used by the body to adapt to lower oxygen availability, or hypoxia, such as that experienced with a moderate increase in altitude. At higher altitudes, the body responds to lower oxygen levels by increasing the availability of HIF, which coordinates the interdependent processes of iron utilization and erythropoietin, or EPO, production to increase RBC production and, ultimately, improve oxygen delivery. 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-PHs are inhibited, allowing HIF to stimulate erythropoiesis. These findings have opened up new possibilities for developing therapeutics, such as HIF-PH inhibitors, which have the potential to treat many diseases.

Our lead product candidate, vadadustat, is a HIF-PH inhibitor, or HIF-PHI, in Phase 3 development for the treatment of anemia due to CKD. Anemia is common in patients with CKD, and its prevalence increases as CKD progresses. Anemia is a condition characterized by abnormally low levels of hemoglobin. Hemoglobin is contained within RBCs and carries oxygen to other parts of the body. If there are too few RBCs or if hemoglobin levels are low, the cells in the body will not get enough oxygen. In patients with CKD, anemia results from inadequate EPO levels, which negatively affect RBC production. In addition, iron, which is essential to RBC production, may be deficient in patients with CKD. Left untreated, anemia significantly accelerates overall deterioration of patient health with increased morbidity and mortality. Based on third party prevalence data and company estimates, approximately 37 million people in the United States have CKD and approximately 5.7 million of these individuals suffer from anemia. Anemia from CKD is currently treated by injectable recombinant human erythropoiesis-stimulating agents, or injectable ESAs, such as EPOGEN® (epoetin alfa) and Aranesp® (darbepoetin alfa), or with iron supplementation or RBC transfusion. Based on publicly available information on ESA sales and market data compiled by a third-party vendor, global sales of injectable ESAs for all uses were estimated to be approximately $7.0 billion in 2016. The vast majority of these sales were for the treatment of anemia due to CKD.

When administered to a patient, injectable ESAs provide supra-physiological levels of exogenous erythropoietin to stimulate production of RBCs. While injectable ESAs can be effective in raising hemoglobin levels, they have the potential to cause significant side effects, and need to be injected subcutaneously or intravenously. In particular, injectable ESAs 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 ESAs. Today, anemia is either not treated or inadequately treated in the majority of non-dialysis dependent, or NDD, CKD patients. There is an unmet need for treatment options that offer an improved safety profile and such agents would have significant market potential.

Vadadustat is designed to stimulate erythropoiesis and effectively treat renal anemia while avoiding the supra-physiologic EPO levels previously observed with injectable ESAs. In addition, vadadustat, if approved, would provide patients with an oral treatment option, rather than an injection. For these reasons, we believe that vadadustat has the potential to set a new standard of care for the treatment of anemia due to CKD.

Phase 1 and Phase 2 data led us to the design of our Phase 3 clinical program for vadadustat. The vadadustat Phase 3 program in NDD-CKD patients with anemia, called PRO_2TECT, and in dialysis dependent, or DD, CKD patients with anemia, called $INNO_2VATE$, is designed to enroll up to approximately 6,900 patients evaluating once daily oral dosing of vadadustat against an injectable ESA active comparator, darbepoetin alfa. The enrollment numbers and the completion of PRO_2TECT and $INNO_2VATE$ will be driven by the accrual 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. As of December 31, 2017, we expect the remaining external aggregate contract research organization, or CRO, costs of PRO_2TECT and $INNO_2VATE$ to be in the range of $420.0 million to $450.0 million. We anticipate reporting top-line clinical data for the PRO_2TECT and $INNO_2VATE$ studies in 2019, subject to the accrual of MACE events. Subject to marketing approvals, we plan to launch vadadustat for the treatment of anemia due to CKD in 2020.

We revised the study designs of FO_2RWARD and TRILO$_2$GY, which we believe will provide additional characterization and differentiation of vadadustat and further strengthen our commercial position if our product candidate is approved. The revised FO_2RWARD study will include once-daily and three-times weekly dosing, data to inform ESA-switching protocols, a larger sample size, and a broader dialysis population that is inclusive of hyporesponders, or patients with anemia due to CKD who are on dialysis and do not adequately respond to injectable ESA. Hyporesponders represent approximately 10-15% of subjects with anemia due to DD-CKD, yet they account for 30-40% of total injectable ESA use. These patients have demonstrated a persistently higher risk of mortality than non-hyporesponders, and represent a high unmet need. Given its differentiated mechanism of action, we believe that vadadustat may provide a treatment option for these patients. The revised TRILO$_2$GY study will include once-daily and three-times weekly dosing and an ESA control, a larger sample size, and a design that can generate data to inform switching from Epogen®, Aranesp® and Mircera®.

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 the United States. We also granted Otsuka exclusive rights to commercialize vadadustat in Europe, China and certain other markets, subject to marketing approvals. In Japan and certain other countries in Asia, we granted Mitsubishi Tanabe Pharma Corporation, or MTPC, exclusive rights to commercialize vadadustat, subject to marketing approvals. In May 2017, we entered into an exclusive license agreement with Vifor (International) Ltd., or Vifor Pharma, to sell vadadustat solely to Fresenius Kidney Care Group LLC, or FKC, dialysis clinics in the United States subject to approval by the FDA and inclusion of vadadustat in a bundled reimbursement model. During the term of the license agreement, Vifor Pharma may not sell to FKC or its affiliates any HIF product that competes with vadadustat in the United States.

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 as well as in-licensed product candidates, such as AKB-5169. In February 2017, we signed an exclusive agreement with Janssen Pharmaceutica NV, or Janssen, a subsidiary of Johnson & Johnson, 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, or IBD. We intend to complete further preclinical development of this compound, and we are targeting submitting an Investigational New Drug application, or IND, to the FDA in 2018.

Upcoming Milestones

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. As illustrated in the table below, CKD patients are categorized in one of five stages based on 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 detailed in the table below, based on prevalence, CKD is estimated to affect approximately 37 million people in the United States. Additionally, the prevalence of anemia increases with the severity of CKD from an estimated 20% in Stage 3 non-dialysis to an estimated 95% in Stage 5 dialysis.

Stages and Prevalence of Chronic Kidney Disease in the United States

Stage	Description	GFR (mL/min/1.73m^2)[a]	U.S. Prevalence Rates[b, c]	Estimated Number of U.S. Patients (millions)[d, e]
1	Kidney damage with normal or increased GFR	≥90	4.6%	11.2
2	Kidney damage with mildly decreased GFR	60-89	3.0%	7.3
3	Moderately decreased GFR	30-59	6.7%	16.4
4	Severely decreased GFR	15-29	0.4%	1.0
5	Kidney failure (includes non-dialysis, dialysis and transplant)	<15 (or dialysis)	0.3% (calculated)	0.7

Sources:

[a] GFR categories defined in the August 2012 Kidney Disease Improving Global Outcomes Clinical Practice Guideline for Anemia in Chronic Kidney Disease, p. vii.

[b] U.S. Prevalence Rates for Stages 1-4 based on averages of data from 2011-2012 and 2013-2014, CDC CKD Surveillance System, National Health and Nutrition Examination Survey, or NHANES.

[c] U.S. Prevalence Rate for Stage 5 is based on a calculation using estimated number of U.S. patients with Stage 5 CKD from 2017 U.S. Renal Data System Annual Report, as set forth in this table, and U.S. population data for people 20 years and older from www.census.gov.

[d] Estimated Number of U.S. Patients for Stages 1-4 based on the 2017 U.S. Prevalence rates, as set forth in this table, as applied by the Company to U.S. population data for people 20 years and older from www.census.gov.

[e] Estimated Number of U.S. End-Stage Renal Disease Patients from 2017 U.S. Renal Data System Annual Report.

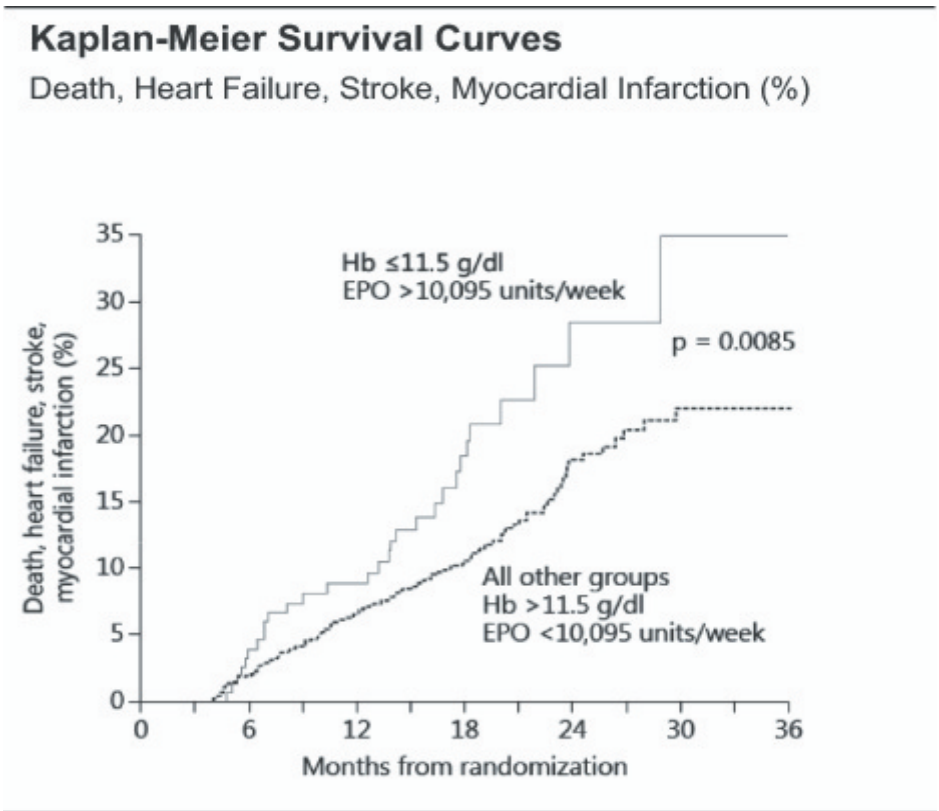
The prevalence and incidence of CKD is increasing in all segments of the United States population. Risk factors for the development of CKD include concomitant diseases such as hypertension, diabetes mellitus and cardiovascular disease, lifestyle factors such as tobacco use and inactivity, family history, aging and prenatal factors such as maternal diabetes mellitus, low birth weight and small-for-gestational-age status. According to an article in *The Lancet* 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 ESAs 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 was published on the risks of injectable ESA use by these patients, forcing physicians to balance serious safety concerns against the efficacy of injectable ESAs. The well-documented safety concerns associated with the use of injectable ESAs include increased cardiovascular risk and the potential for increased rate of tumor progression in patients with cancer[1].

As a result of the safety concerns related to injectable ESA use, patients live with lower hemoglobin levels, higher rates of RBC transfusions, and receive more intravenous iron, or IV iron, to treat anemia due to CKD. IV iron and RBC transfusions also subject patients to safety risks. 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 ESA doses had better outcomes than patients receiving higher injectable ESA doses despite lower achieved hemoglobin levels. Therefore, higher injectable ESA doses, not the achieved hemoglobin level, appeared to be most strongly correlated with adverse outcomes.



Source:
McCullough P.A. · Barnhart H.X. · Inrig J.K. · Reddan D. · Sapp S. · Patel U.D. · Singh A.K. · Szczech L.A. · Califf R.M. Am J Nephrol 2013;37:549-558 (DOI:10.1159/000351175);
Permission granted by S. Karger AG, Basel.

[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.

Vadadustat Has the Potential to Set a New Standard of Care

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

Vadadustat stimulated endogenous EPO production. In two Phase 1 studies in normal healthy volunteers and one Phase 2 study in CKD patients, vadadustat increased serum EPO levels in a dose-dependent manner. Pre-dose EPO levels returned to baseline levels prior to subsequent daily dose.

Vadadustat significantly increased and maintained hemoglobin levels. Our Phase 2 studies in CKD subjects with anemia demonstrated that vadadustat significantly increased and/or maintained hemoglobin levels.

Vadadustat was dosed orally once daily and three-times weekly. Phase 2 studies have shown that vadadustat can be orally dosed once daily in NDD-CKD subjects over 20 weeks of dosing. In addition, a Phase 2 clinical study in DD-CKD subjects demonstrated that in subjects who remained on therapy, once daily or three-times weekly oral dosing of vadadustat maintained stable hemoglobin levels in subjects converting from injectable ESA therapy over 16 weeks.

Vadadustat resulted in favorable changes in iron parameters. In three Phase 2 clinical studies, treatment with vadadustat was associated with decreases in ferritin and hepcidin and increases in total iron binding capacity. These changes are consistent with improved iron mobilization and utilization for erythropoiesis in NDD-CKD and DD-CKD subjects.

For the above reasons, we believe that vadadustat has the potential to stimulate erythropoiesis while demonstrating a reduced risk of cardiovascular and thrombotic events compared to injectable ESAs. These cardiovascular and thrombotic 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 cardiovascular and thrombotic adverse events associated with vadadustat as compared with darbepoetin alfa, an injectable ESA, is being assessed in the global Phase 3 program for vadadustat.

Market Potential

We believe there is significant market opportunity for an oral HIF-based product, such as vadadustat, to potentially treat dialysis and non-dialysis patients with anemia due to CKD, some of whom are receiving injectable ESA therapy and many of whom are not due to the safety concerns and other barriers to treatment associated with injectable ESAs.

We estimate that approximately 400,000-450,000 U.S. dialysis patients are currently receiving some injectable ESA treatment for anemia due to CKD. According to the 2017 U.S. Renal Data System, or USRDS, Annual Data Report, there are approximately 438,000 US patients on hemodialysis and 49,000 patients on peritoneal dialysis, with approximately 90% of patients and 75% of patients receiving ESA therapy, respectively.

Data from the 2015 USRDS Annual Data Report indicate that the collective injectable ESA treatment rate in NDD-CKD patients decreased by approximately half from 2009 to 2013, following the emergence of cardiovascular safety concerns associated with injectable ESAs and kidney disease guideline updates. This change in injectable ESA treatment rate suggests there is potential to treat a large patient population with HIF-based products who are not receiving injectable ESAs today. Moreover, many patients are not treated with an injectable ESA even though their hemoglobin concentration is below the ESA treatment initiation threshold suggested by the Kidney Disease Improving Global Outcomes, or KDIGO.

HIF-PH Inhibition: A Mechanism of Action That Is Designed to Mimic the Body's Physiologic Response to Hypoxia

Vadadustat is designed to work by a mechanism of action that differs from injectable ESAs. This mechanism of action is referred to as HIF-PH inhibition. HIF is the primary regulator of the production of RBCs and is responsible for orchestrating the body's physiologic 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, a normal biological process known as erythropoiesis, and enhancement of the delivery of iron to the bone marrow, ensuring the incorporation of iron into hemoglobin to support erythropoiesis. HIFα is constitutively expressed in the cytoplasm but broken down immediately under normal oxygen conditions by the HIF-PHα enzymes. Inhibition of these enzymes allows HIFα concentrations to build and translocate to the nucleus to initiate hypoxic gene transcription, where it binds to the HIFß protein. When bound together, HIFα and HIFß stimulate erythropoiesis and iron transfer proteins. With continued stabilization of the HIFα protein either by staying at higher altitude or by the administration of a HIF-PHI, the level of hemoglobin and RBCs will rise in order to increase the amount of oxygen circulating in the blood.

Vadadustat Clinical Development Overview

The following 17 studies of vadadustat have evaluated the safety, tolerability, pharmacokinetic and pharmacodynamic properties of vadadustat and supported further clinical development:

nine completed Phase 1 studies in normal 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 subjects with anemia (CI-0009);

five completed Phase 2 studies in NDD-CKD subjects with anemia (CI-0003, CI-0004, CI-0005, CI-0007, CI-0021); and

two completed Phase 2 studies in DD-CKD subjects with anemia (CI-0011, CI-0022).

The results from three of these studies are summarized below.

Vadadustat Clinical Development Summary

Findings from two clinical studies demonstrated that vadadustat stimulated endogenous EPO production while avoiding excessive increases, achieved the desired outcomes of raising and maintaining hemoglobin, and increased iron mobilization to support erythropoiesis. Vadadustat's safety profile has generally been consistent across Phase 1 and 2 studies completed to date. The common adverse events, or AEs, and serious adverse events, or SAEs, for the respective studies are discussed below.

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

We 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. Mean serum EPO levels increased by 39%, 69%, and 86% over baseline, at 16 hours after dosing in the vadadustat 500 mg/day, 700 mg/day, and 900 mg/day dosing groups, respectively, and returned to baseline by 24 hours after dosing. The incidence of AEs was generally similar between the combined vadadustat dosing groups, which was 76.5%, and the placebo group, which was 78%. Gastrointestinal AEs occurred in 26.5% of subjects in the vadadustat groups and in no subjects on placebo, of which mild to moderate diarrhea was the most frequent at 16.7%, with evidence of a dose-related effect. No SAEs or deaths were reported in this study.

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

We completed a multi-center Phase 2b study of vadadustat in non-dialysis subjects with anemia due to 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 stages 1 to 5. Subjects were enrolled into one of three groups: (1) injectable ESA naïve with hemoglobin ≤10.5 g/dL, (2) previously treated with injectable ESA with hemoglobin ≤10.5 g/dL, or (3) actively treated with injectable ESA with hemoglobin ≥9.5 and ≤12.0 g/dL, and were randomized at a rate of 2 to 1 to once daily vadadustat or placebo. The primary endpoint was the percentage 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 variations of hemoglobin from baseline, known as hemoglobin excursions, of ≥13 g/dL.

The average age of subjects was 66 years; approximately 75% of subjects had diabetes mellitus; and the mean estimated GFR 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. Between Groups 1 and 2 (the two correction cohorts; ESA-naïve and ESA previously treated), mean Hb increased significantly in the vadadustat group from pre-dose average to end-of-study average (Week 19/20). In Group 3 (conversion cohorts; ESA actively treated), 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 preceded by an increase in reticulocytes and accompanied by an increase in total iron binding capacity 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 an AE in the vadadustat and placebo treatment groups (vadadustat 74.6% vs. placebo 73.6%); however, the frequency of certain AEs - diarrhea, nausea, hypertension and hyperkalemia - was greater in the vadadustat arm compared to placebo. In the vadadustat arm, a higher number of subjects reported SAEs of acute and chronic renal failure compared to

placebo (9.4% vs. 2.8%, respectively); however, none were considered drug-related by the investigator. The percentage of subjects who had an SAE resulting in dialysis initiation, an objective measure of the severity of renal disease, was comparable between vadadustat and placebo groups (8.0% versus 9.7%, respectively) and the number of subjects who discontinued from the study due to AEs of worsening CKD requiring dialysis was also comparable between the vadadustat (4.3%) and placebo (5.6%) groups. There were three deaths in vadadustat-treated subjects of which 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 assess relatedness. 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 Subjects (CI-0011)

We 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 with baseline hemoglobin levels of 9-12 g/dL, who were maintained on injectable ESAs prior to study entry. Subjects were converted from injectable ESA to vadadustat, and assigned to one of three dose cohorts: 300 mg once daily; 450 mg once daily; or 450 mg three-times weekly. For each dose cohort, the 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 8, the dose of vadadustat could be increased or decreased to maintain hemoglobin levels as needed. Intravenous iron use was allowed.

The underlying demographics and profiles of these CKD subjects 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 at 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.

For subjects in all three dosing cohorts (converted from ESA) who completed the study, the primary endpoint of maintaining stable mean hemoglobin levels over 16 weeks was achieved. 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.

Adverse events were balanced across the three cohorts. There were no discernible trends in the frequency of AEs or SAEs by dose cohort. The most frequently reported AEs were nausea and diarrhea with no apparent dose relationship. The majority of AEs were mild or moderate in severity. SAEs were reported in 13 subjects, or 13.8%; no SAEs were reported as related to vadadustat and no deaths occurred during the study. Reported events appear to be consistent in frequency and severity with previous clinical experience and co-morbidities described in medical literature in subjects with CKD. 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 two global Phase 3 studies to support an indication for the treatment of anemia in DD-CKD patients, the details of which are below. In addition, we plan to initiate another Phase 3 DD-CKD study, known as TRILO$_2$GY, in late 2018 or early 2019.

> 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) (PRO$_2$TECT - CORRECTION)”
>
> 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) (PRO$_2$TECT - CONVERSION)”

CI-0016: “Phase 3, Randomized, Open-Label, Active-Controlled Study Evaluating the Efficacy and Safety of Oral Vadadustat for the Correction or Maintenance Treatment of Anemia in Subjects with Dialysis-Dependent Chronic Kidney Disease (DD-CKD) (INNO$_2$VATE – CORRECTION/ CONVERSION)”

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) (INNO$_2$VATE - CONVERSION)”

In both the PRO$_2$TECT and INNO$_2$VATE Phase 3 programs, the primary efficacy endpoint is the mean change in hemoglobin between baseline, which is the mean pretreatment hemoglobin, and the primary evaluation period, concluding non-inferiority, or NI, when the upper 95% confidence interval of the hazard ratio of vadadustat to darbepoetin alfa does not exceed the NI margin. Both the PRO$_2$TECT and INNO$_2$VATE programs will include the primary safety endpoint of the assessment of 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 of vadadustat to 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 up to approximately 6,900 CKD subjects. We have engaged IQVIA, formerly known as Quintiles IMS, as our primary clinical CRO for the PRO$_2$TECT and INNO$_2$VATE programs. As of December 31, 2017, we expect the remaining external aggregate CRO costs of the PRO$_2$TECT and INNO$_2$VATE programs to be in the range of $420.0 million to $450.0 million. Such estimated costs could increase significantly if PRO$_2$TECT and INNO$_2$VATE takes longer to complete or if we choose to add additional investigative sites, add additional patients, modify the clinical trial protocol, or perform other studies in support of PRO$_2$TECT and INNO$_2$VATE.

We plan to initiate a Phase 3 study, TRILO$_2$GY, based on the results of our 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 injectable ESA therapy and remained on therapy. We had planned to initiate TRILO$_2$GY in early 2018 but have since revised the study design, and now expect initiation in late 2018 or early 2019, with top-line data expected in early 2020. The revised study design will include once-daily and three-times weekly dosing and an ESA control, a larger sample size, and a design that can generate data to inform switching from Epogen®, Aranesp® and Mircera®. We believe this new study design will provide additional characterization and differentiation of vadadustat and further strengthen our commercial position if the drug is approved.

Additional Studies

We have completed a thorough QT, or TQT, study in accordance with FDA guidance. The study showed that vadadustat does not alter cardiac repolarization intervals in normal healthy volunteers following a single dose of up to 1,200 mg. In addition, a drug-drug interaction, or DDI, study was conducted to evaluate the effect of vadadustat on celecoxib, a substrate for the hepatic cytochrome P450 enzyme CYP2C9. Based on this study it was concluded that vadadustat does not inhibit CYP2C9 to any appreciable extent. Therefore, no clinically significant effect of vadadustat on drugs that are CYP2C9 substrates, for example statins such as losartan or rosuvastatin, would be expected through this specific mechanism. Additional DDI studies are planned.

Subsequent to our initiation of our Phase 2 study, FO$_2$RWARD, in May 2017, we closed this study and revised its design, which we believe will provide additional characterization and differentiation of vadadustat and further strengthen our commercial position if the drug is approved. The new FO$_2$RWARD study replaces the former one and will include once-daily and three-times weekly dosing, data to inform ESA-switching protocols, a larger sample size, and a broader dialysis population that is inclusive of hyporesponders, or patients with anemia due to CKD who are on dialysis and do not adequately respond to injectable ESA. Hyporesponders represent approximately 10-15% of subjects with anemia due to DD-CKD, yet they account for 30-40% of total injectable ESA use. These patients have demonstrated a persistently higher risk of mortality than non-hyporesponders, and represent a high unmet need. Given its differentiated mechanism of action, we believe that vadadustat may provide a treatment option for these patients. We expect to initiate the study in the second quarter of 2018, with top-line data expected in late 2018 or early 2019.

Manufacturing and Supply

We neither own nor operate, and currently have no plans to own or operate, any manufacturing facilities. We currently rely on third-party contract manufacturing organizations, or CMOs, to produce all of our preclinical and clinical material supply. We expect to continue to rely on either existing or alternative CMOs to supply our ongoing and planned preclinical and clinical studies and for commercial production.

We have established relationships with several CMOs under which the CMOs have manufactured preclinical and clinical supplies of vadadustat drug substance and drug product. All clinical supplies are manufactured under current Good Manufacturing Practices, or cGMPs, which is a regulatory standard for the production of pharmaceuticals that will be used in humans. We currently have redundant supply arrangements in place for the preclinical and clinical supply of vadadustat. We intend to put supply agreements in place for commercial manufacturing of vadadustat at the appropriate time. We plan to mitigate potential commercial supply risks for vadadustat, if any, through inventory management and redundant manufacturing arrangements for both drug substance and drug product; however, the timing of such arrangements is uncertain and may occur following the launch of vadadustat, if approved. The drug substance and drug product for AKB-5169 are supplied to us from single source suppliers with limited capacity.

Vadadustat is a small molecule. The synthesis of vadadustat is reliable and reproducible from starting materials available from multiple sources at commercially relevant scale using no unusual manufacturing equipment. Vadadustat can be readily formulated into compressed tablets with standard ingredients using common manufacturing processes.

Strategic Collaborations and Other Significant Agreements

U.S. Collaboration with Otsuka Pharmaceutical Co. Ltd.

On December 18, 2016, we entered into a collaboration and license agreement with Otsuka, or the Otsuka U.S. Agreement, pursuant to which we agreed to co-exclusively collaborate with Otsuka with respect to the development and commercialization of vadadustat in the United States, subject to the approval of vadadustat by the FDA. We continue to lead the ongoing global Phase 3 development program for vadadustat, and control and retain final decision-making authority with respect to all development of vadadustat, subject to the terms of our other collaboration agreements.

Under the terms of the Otsuka U.S. Agreement, Otsuka paid us an upfront payment of $125.0 million and we expect Otsuka to provide additional funding of $153.6 million or more, depending on the actual costs incurred, 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 $190.0 million in development and regulatory milestones and up to $575.0 million in specified commercial milestones.

The Otsuka U.S. Agreement establishes a profit share for the commercialization of vadadustat in the United States. 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. Under the terms of the Otsuka U.S. Agreement, Otsuka had an option to convert the profit share arrangement into a right to receive mid-single digit royalties on net sales of vadadustat; however, on August 4, 2017, Otsuka waived its right to exercise its conversion option in advance of the option's expiration.

Under the Otsuka U.S. Agreement, we and Otsuka will jointly conduct, and will have equal responsibility for, all medical affairs and commercialization activities pursuant to plans agreed by the parties. We will remain responsible for manufacturing vadadustat.

International Collaboration with Otsuka Pharmaceutical Co. Ltd.

On April 25, 2017, we entered into a collaboration and license agreement with Otsuka, or the Otsuka International Agreement, pursuant to which we granted Otsuka an exclusive license for the development and commercialization of vadadustat. The territory covered by the Otsuka International Agreement includes the European Union, Russia, China, Australia, Canada, the Middle East and certain other countries, or the Otsuka International Territory, but excludes Latin America and previously licensed jurisdictions. Under the Otsuka International Agreement, Otsuka will be responsible for certain development activities and commercializing vadadustat in the Otsuka International Territory, while we will continue to lead the ongoing global Phase 3 development program. Otsuka will fund a significant percentage of the costs of such global development program regardless of the total actual costs ultimately incurred. We retain final decision-making authority with respect to the manufacture and supply of vadadustat in the Otsuka International Territory, the global Phase 3 development program, and the global brand strategy for vadadustat. Otsuka will have final decision-making authority with respect to certain development activities and commercialization matters in the Otsuka International Territory.

Under the terms of the Otsuka International Agreement, we expect Otsuka to pay us at least $236.6 million, comprised of $73.0 million that was paid upon execution of the Otsuka International Agreement and $163.6 million or more, depending on actual costs incurred, of development funding. In addition, we are eligible to receive from Otsuka up to $132.0 million in development and regulatory milestones and up to $525.0 million in commercial milestones. Otsuka also agreed to make tiered, escalating royalty payments ranging from low double digits up to thirty percent of net sales of vadadustat within the Otsuka International Territory. In limited circumstances, upper tier royalties may be subject to reduction if the supply price charged by us to Otsuka for vadadustat exceeds certain agreed upon thresholds. Otsuka may elect to conduct additional studies of vadadustat in the European Union, subject to our right to delay such studies based on our objectives outside the Otsuka International Territory. Otsuka will pay a percentage of the costs of any such studies, and we will pay its portion of the costs in the form of a credit against future amounts due to us under the Otsuka International Agreement.

Collaboration with Mitsubishi Tanabe Pharma Corporation

On December 11, 2015, we entered into a collaboration agreement with MTPC, or the MTPC Agreement, providing MTPC with exclusive development and commercialization rights to vadadustat in Japan and certain other Asian countries, or the MTPC Territory. In addition, we will supply vadadustat for both clinical and commercial use in the MTPC Territory, subject to MTPC's option to manufacture commercial drug product in the MTPC Territory.

We and MTPC agreed that, instead of including Japanese patients in our global Phase 3 program for vadadustat, MTPC would be the sponsor of a Phase 3 program for vadadustat in Japan. Following consultation with the Japanese Pharmaceuticals and Medical Devices Agency, or the PMDA, MTPC initiated its Phase 3 development program for vadadustat in Japan in the fourth quarter of 2017.

Under the terms of the MTPC Agreement, MTPC will make payments to us of up to $245.0 million in the aggregate based on the achievement of certain development, regulatory and sales milestones, as well as tiered double-digit royalty payments of up to 20% on sales of vadadustat in the MTPC Territory. MTPC is responsible for the costs of the Phase 3 program for vadadustat in Japan and will make no additional funding payments for our global Phase 3 program vadadustat. Additionally, the development costs of approximately $21.4 million for our Phase 2 studies in Japan are reimbursable by MTPC.

In addition, in September 2017, we agreed to provide MTPC with an option to access data from our global Phase 3 vadadustat program for payments to us of up to $25.0 million.

Vifor Pharma License Agreement

On May 12, 2017, we entered into a License Agreement with Vifor Pharma, or the Vifor Agreement, pursuant to which we will grant Vifor Pharma an exclusive license to sell vadadustat solely to FKC, an affiliate of Fresenius Medical Care North America, in the United States.

The parties' rights under the Vifor Agreement are conditioned upon the approval of vadadustat for DD-CKD patients by the FDA, inclusion of vadadustat in a bundled reimbursement model, and payment by Vifor Pharma of a $20 million milestone upon the occurrence of these two events. The Vifor Agreement is structured as a profit share arrangement between us and Vifor Pharma in which we will receive a majority of the profit from Vifor Pharma's sales of vadadustat to FKC in the United States. We will share the milestone payment and the revenue from the profit share with Otsuka pursuant to the Otsuka U.S. Agreement. We retain all rights to commercialize vadadustat for use in the NDD-CKD market and in other dialysis organizations in the United States, which will be done in collaboration with Otsuka if approved by the FDA.

Prior to FDA approval of vadadustat, we and Vifor Pharma will enter into a commercial supply agreement for vadadustat pursuant to which we will supply all of Vifor Pharma's requirements for vadadustat in the United States. In addition, Vifor Pharma will enter into a supply agreement with FKC that will govern the terms pursuant to which Vifor Pharma will supply vadadustat to FKC for use in patients at its dialysis centers. During the term of the Vifor Agreement, Vifor Pharma will not sell to FKC or its affiliates any HIF product that competes with vadadustat in the United States.

Janssen Pharmaceutica NV Research and License Agreement

On February 9, 2017, we entered into a Research and License Agreement with Janssen, which granted us an exclusive license under certain intellectual property rights to develop and commercialize worldwide certain HIF-PH-targeted compounds.

Under the terms of the Janssen Agreement, Janssen granted us a license for a three-year research term to conduct research on Janssen's 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 cost and expense. The Janssen Agreement includes a license to develop and commercialize AKB-5169, a preclinical compound in development as an oral treatment for IBD.

Under the terms of the Janssen Agreement, we paid an upfront payment of $1.0 million in cash to Janssen and issued a warrant to purchase 509,611 shares of our common stock, the fair value of which was approximately $3.4 million. 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.

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 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."

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 six issued patents covering the composition of matter, polymorph, method of treating anemia, and pharmaceutical compositions of vadadustat 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, Israel and India. The expected expiration dates for these patents are between 2027 and 2034 plus any extensions or adjustments of term available under national law.

In July 2011, a third party filed an opposition to our issued European Patent No. 2044005, or the '005 EP Patent. During the oral proceedings, which took place on April 10, 2013, the Opposition Division of the European Patent Office maintained the '005 EP

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 appealed the decision of the Opposition Division. On February 27, 2018, we withdrew the ’005 EP Patent from appeal and filed a divisional patent application to pursue a focused claims set that includes claims for vadadustat, as well as pharmaceutical compositions and methods of treating anemia. We cannot be assured that such claims in the divisional patent application will be granted by the European Patent Office. If such claims are not granted, or the scope of the claims is significantly narrowed, we may not be able to adequately protect our rights, provide sufficient exclusivity, or preserve our competitive advantage.

We also hold patents and patent applications directed to processes for manufacturing vadadustat, dosing regimens, formulations, and various other aspects relating to the treatment of anemia using vadadustat that are expected to expire between 2032 and 2036 exclusive of possible patent term extensions or adjustments.

AKB-5169 Patent Portfolio

There is one issued patent and two pending patent applications 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 dates for these patents are between 2029 and 2038 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 will prevent us from commercializing vadadustat in the United States for the treatment of anemia due to CKD; 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 filed an opposition in Europe against FibroGen’s European Patent No. 1463823, or the ’823 EP Patent, and 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 two to three 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 JP Patent, which is the Japanese counterpart to the ’823 EP 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 ’131 JP 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 EP Patent and ’131 JP Patents. In the event FibroGen were to obtain such a patent in the United States, we may decide to challenge the patent as 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. 2322155, or the '155 EP Patent, 1633333, or the '333 EP Patent, and 2322153, or the '153 EP Patent requesting the patents be revoked in their entirety. These related patents claim, among other things, various compounds that either stabilize HIFα 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 our collaborators with maximum flexibility for developing vadadustat and our pipeline of HIF-PHIs.

Oppositions to the '155 EP Patent and the '153 EP Patent were also filed by Glaxo Group Limited, or Glaxo, and by Bayer Intellectual Property GmbH, Bayer Pharma Aktiengesellschaft, and Bayer Animal Health GmbH, or collectively Bayer.

With regards to the opposition that we filed in Europe against the '333 EP Patent, an oral proceeding took place on 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. On December 9, 2016, FibroGen filed a notice to appeal the decision to revoke the '333 EP Patent.

In oral proceedings held on May 29, 2017, regarding the '155 EP Patent, the European Opposition Division ruled that the '155 EP Patent as granted did not meet the requirements for patentability under the European Patent Convention and, therefore, revoked the patent in its entirety. FibroGen filed a notice to appeal the decision to revoke the '155 EP Patent on May 29, 2017.

Subsequently, in related oral proceedings held on May 31, 2017 and June 1, 2017 for the '153 EP Patent, the European Opposition Division maintained the patent after FibroGen significantly narrowed the claims to an indication for which vadadustat is not intended to be developed. We and Glaxo separately filed notices to appeal the decision to maintain the '153 EP Patent on November 9, 2017. Bayer filed a notice to appeal the decision on November 14, 2017.

Competition

If vadadustat is approved and launched commercially, competing drugs may include EPOGEN® (epoetin alfa) and Aranesp® (darbepoetin alfa), both commercialized by Amgen, Procrit® (epoetin alfa), Eprex® (epoetin alfa), commercialized by Johnson & Johnson, and Mircera® (methoxy PEG-epoetin beta), commercialized by Vifor Pharma in the United States and Roche Holding Ltd. outside the United States. In Europe and other markets biosimilar versions of injectable ESAs are available and may become available in the United States in the future. We may also 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, Japan Tobacco International is currently in Phase 3 clinical development of its product candidate, JTZ-951, in Japan. GlaxoSmithKline's product candidate, daprodustat, is also in Phase 3 clinical studies and Bayer HealthCare AG is currently in Phase 3 clinical development of its product candidate, molidustat, in Japan. Some of these product candidates may launch in certain markets as early as 2019. In addition, certain companies are developing potential new therapies for renal-related diseases that could potentially reduce injectable ESA utilization and thus limit the market potential for vadadustat if they are approved and launched commercially. Other new therapies are in development for the treatment of conditions inclusive of renal anemia that may impact the market for anemia-targeted treatment.

Regulatory Matters

The FDA, and comparable regulatory authorities in other countries, impose substantial and extensive requirements upon companies involved in the research, manufacture, recordkeeping, labeling and packaging, storage, distribution, approval, post-approval monitoring and reporting, marketing, advertising and promotion, sampling, pricing, and export and import of drugs. The process of obtaining marketing 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, 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 U.S. 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, 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 Investigational New Drug application, or IND, 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, 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 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, preclinical 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.

Preclinical 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 preclinical tests, together with manufacturing information, analytical data and a proposed clinical trial protocol, and other information, are submitted to FDA as part of an IND. The central focus of an IND submission is on the general investigational plan and the protocol for first-in-human study. Some preclinical 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 current 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 involving subjects in the United States must be submitted to the FDA as part of the IND. In addition, an 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.

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 the United States

In addition to regulations in the United States, we are subject to a variety of regulations in other jurisdictions governing, among other things, the conduct of clinical trials, and the import, export and distribution of drugs used in clinical trials. 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, marketing and marketing approvals, and pricing and reimbursement requirements 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.

In the European Union, marketing authorization for a medicinal product can be obtained through a centralized, decentralized, or mutual recognition procedure.

In accordance with the centralized procedure, the applicant can submit a single marketing authorization application, or MAA, to the European Medicines Agency, or EMA. If granted, a centralized marketing authorization permits the marketing of a product in all 28 member states of the European Union, or EU Member States, and three of the four European Free Trade Association, or EFTA, States (Iceland, Liechtenstein and Norway). The centralized procedure is mandatory for certain medicinal products, including orphan medicinal products, medicinal products derived from certain biotechnological processes, advanced therapy medicinal products and certain other medicinal products containing a new active substance for the treatment of certain diseases, and is optional for certain other products, including medicinal products that are a significant therapeutic, scientific or technical innovation, or whose authorization would be in the interest of public or animal health at EU level.

Unlike the centralized authorization procedure, the decentralized marketing authorization procedure requires a separate application to, and leads to separate approval by, the competent authorities of each EU Member State in which the product is to be marketed.

A mutual recognition procedure is used when a product is already authorized in at least one EU Member State and the marketing authorization holder wishes to obtain a marketing authorization for the same product in at least one other EU Member State.

An approved Pediatric Investigation Plan, or PIP, is required in Europe prior to submission of the MAA covering all subsets of the pediatric population, unless the EMA has granted (1) a product-specific waiver, (2) a class waiver or (3) a deferral for one or more of the measures included in the PIP. 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. 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.

The process of obtaining approval for a new drug in Japan resembles U.S. and EU procedures in both substance and scope. All NDAs are collected and reviewed by the PMDA. PMDA review typically involves at least two formal evaluations to establish the safety and efficacy of the drug candidate, as well as one cGMP facility inspection. Consultations to correct outstanding issues are conducted as needed. Assuming satisfactory results, these reports are communicated to the Ministry of Health, Labour, and Welfare, or MHLW, which then issues a final approval of the drug.

Regulatory Data Protection in the European Union

In the European Union, innovative medicinal products approved on the basis of a complete independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity pursuant to Directive 2001/83/EC. Regulation (EC) No 726/2004 repeats this entitlement for medicinal products authorized in accordance the centralized authorization procedure. Data exclusivity prevents applicants for approval of generics of these innovative products from referencing the innovator's data to assess an Abbreviated New Drug Application for a period of eight years. During an additional two-year period of market exclusivity, a generic marketing authorization application can be submitted and authorized, and the innovator's data may be referenced, but no generic medicinal product can be marketed in the European Union until the expiration of the market exclusivity. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the

marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity so that the innovator gains the prescribed period of data exclusivity, another company nevertheless could also market another version of the product if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

Periods of Authorization and Renewals

A marketing authorization has an initial validity for five years in principle. The marketing authorization may be renewed after five years on the basis of a re-evaluation of the risk-benefit balance by the EMA or by the competent authority of the EU Member State. To this end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. The European Commission or the competent authorities of the EU member states may decide, on justified grounds relating to pharmacovigilance, to proceed with one further five-year period of marketing authorization. Once subsequently definitively renewed, the marketing authorization shall be valid for an unlimited period. Any authorization which is not followed by the actual placing of the medicinal product on the European Union market (in case of centralized procedure), or on the market of the authorizing EU Member State, within three years after authorization ceases to be valid.

Regulatory Requirements Post Marketing Authorization

After an authorization for a medicinal product in the European Union is obtained, the holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These include:

compliance with the European Union's stringent pharmacovigilance or safety reporting rules, these rules may require post-authorization studies or additional monitoring obligations; and

the manufacturing of authorized medicinal products, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the applicable European Union laws, regulations and guidance.

Brexit and the Regulatory Framework in the United Kingdom

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. Thereafter, on March 29, 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Treaty of Lisbon. The United Kingdom is thus due to exit the European Union on March 29, 2019. Since the regulatory framework for pharmaceutical products in the United Kingdom covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from European Union directives and regulations, Brexit could materially impact the future regulatory regime which applies to products and the approval of product candidates in the United Kingdom. It remains to be seen how, if at all, Brexit will impact regulatory requirements for product candidates and products in the United Kingdom.

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 subjects 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 subject population to evaluate dosage tolerance, appropriate dosage as well as dosing strategies, identify possible adverse effects and safety risks, and evaluate preliminarily the efficacy of the drug for specific targeted indications in subjects with the disease or condition under study.

Phase 3 clinical trials are typically conducted after 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 subjects, 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 subject population at multiple, geographically-dispersed clinical trial sites.

Phase 4 clinical trials are conducted following FDA approval of a product. In some cases, FDA may condition approval of an NDA for a product 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.

The FDA, the IRB, or the sponsor may suspend or discontinue a clinical trial at any time for various reasons, 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 its review of 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 preclinical 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 may be extended. The first indication of the FDA's review progress is provided at the mid-cycle review meeting. This typically occurs five months after the NDA is accepted for review. However, the review process can be 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 cGCP requirements is satisfactory.

After the FDA evaluates the NDA and conducts inspections of manufacturing facilities, it may issue either an approval letter or a Complete Response Letter, or 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, preclinical 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 potential safety risks, which could include medication guides, physician communication plans, restricted distribution programs, patient registries, or other mechanisms to try to reduce the risks of use in patients. 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 marketing 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. In addition, the FDA strictly regulates labeling, advertising, promotion and other types of information on products that are placed on the market. As a general matter, 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 consistent 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, untitled 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 preclinical studies and clinical trials. As with new NDAs, the review process is often significantly extended by 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 impose 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 on their quality control processes to maintain compliance with cGMP requirements 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. Preclinical and clinical data may be interpreted by the FDA in different ways, which could delay, limit or prevent marketing 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.

The policies of the FDA and of other regulatory authorities may change and additional government regulations may be enacted that could prevent, limit, or delay marketing approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the U.S. or in other regions.

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, or HHS, Centers for Medicare & Medicaid Services, or CMS, HHS 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.

In 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 the marketing and sale of any of our products. Anti-kickback laws generally prohibit a pharmaceutical manufacturer from knowingly and willfully 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 willfully 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 manufacturers' interactions with healthcare providers.

Similarly, outside the United States, a number of countries have implemented laws, or their industry associations have recommended codes, restricting interactions between pharmaceutical manufacturers with marketed products and healthcare providers or requiring disclosure of transfers of value made by such pharmaceutical manufacturers to healthcare providers. For example, countries with disclosure laws include France and Belgium. Industry codes include the code issued by the European Federation of Pharmaceutical Industries and Associations. General anticorruption or antibribery laws may also regulate our interactions with health care providers outside the U.S. and these laws may currently to our activities. See "Regulatory Matters- Laws Relating to Foreign Trade." In addition, most countries outside of the United States prohibit pharmaceutical manufacturers from promoting prescription drugs to members of the general public.

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

Pharmaceutical Pricing and Reimbursement

In both domestic and foreign markets, sales of any product candidates for which we receive marketing 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, private health insurers, including managed care plans, and other organizations. These third-party payors and governmental authorities 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 and thus, may not be approved or reimbursed in certain markets on this basis. Third-party reimbursement may not be available or may not be adequate 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. In order to participate in these programs, we may be required to provide discounted pricing or pay rebates on our products. 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. Even if payors cover our products, the coverage might be subject to various cost containment methods to reduce their costs for drug products, such as copayment and deductible requirements that could deter patients from using our products. The marketability of any products for which we receive marketing approval for commercial sale may suffer if the government and other third-party payors fail to provide adequate coverage and reimbursement.

In the U.S., federal and state governments continue to propose and pass legislation designed to reform delivery of, or payment for, health care, which include initiatives to reduce the cost of health care. For example, in March 2010, the U.S. Congress enacted the Patient Protection and Affordable Care Act and the Health Care and Education Reconciliation Act, or the Healthcare Reform Act, which expanded health care coverage through Medicaid expansion, included a tax penalty on individuals who do not obtain health insurance, or the individual health insurance mandate, and altered the coverage and reimbursement of drug products under government health care programs. Under the current administration, there have been ongoing efforts to modify or repeal all or certain provisions of the Healthcare Reform Act. The current administration may also take executive action in the absence of legislative action. For example, in October 2017, the President announced that his administration will withhold the cost-sharing subsidies paid to health

insurance exchange plans serving low-income enrollees. Tax reform legislation was also enacted at the end of 2017 that includes provisions that will affect healthcare insurance coverage and payment, such as the elimination of the individual health insurance mandate beginning in 2019. The Bipartisan Budget Act of 2018 contained various provisions that affect coverage and reimbursement of drugs, including an increase in the discount that manufacturers of Medicare Part D brand name drugs must provide to Medicare Part D beneficiaries during the coverage gap, which was implemented by the Healthcare Reform Act, from 50% to 70% starting in 2019. The elimination of the individual health insurance mandate and any successful attempts to repeal the Healthcare Reform Act will likely result in fewer Americans having comprehensive healthcare insurance coverage, which could affect the potential use or reimbursement of our products.

Recently, there has been considerable public and government scrutiny in the U.S. of pharmaceutical pricing and proposals to address the perceived high cost of pharmaceuticals. There have also been several recent state legislative efforts to address drug costs, which generally have focused on increasing transparency around drug costs or limiting drug prices or price increases. Adoption of new legislation at the federal or state level could affect demand for, or pricing of, our product candidates if approved for sale. We cannot, however, 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.

Any significant spending reductions affecting Medicare, Medicaid or other publicly funded or subsidized health programs that may be implemented, or any significant taxes or fees that may be imposed on us as part of any broader deficit reduction effort, could have an adverse impact on our anticipated product revenues.

Pharmaceutical Pricing and Reimbursement Outside the U.S.

In many countries, including EU Member States, the pricing of prescription drugs is subject to governmental control. Additional countries may adopt similar approaches to the pricing of prescription drugs. In such 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, especially as part of heightened cost containment measures. Political, economic, and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after coverage and reimbursement have been obtained. Reference pricing used by various countries and parallel distribution, or arbitrage between low-priced and high-priced countries, can further reduce prices. In some countries, we may be required to conduct a clinical study or other studies that compare the cost-effectiveness of any of our product candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval, which is time-consuming and costly. We cannot be sure that such prices and reimbursement will be acceptable to us or our strategic partners. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If pricing is set at unsatisfactory levels or if reimbursement of our products is unavailable or limited in scope or amount, our revenues from sales by us or our strategic partners and the potential profitability of any of our product candidates in those countries would be negatively affected.

Laws Relating to Foreign Trade

We are subject to various federal and foreign laws that govern our international business practices. These 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. Additionally, interactions with or on the part of our partners, collaborators, contract research organizations, vendors or other agents may also implicate the FCPA. 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. Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents unique challenges in the pharmaceutical industry because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments made by pharmaceutical companies to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Our international operations could also be subject to compliance with national laws of other countries, such as the United Kingdom Bribery Act. of 2010, or U.K. Bribery Act. The U.K. Bribery Act applies to any company "carrying on business" in the United Kingdom, irrespective of where the offending conduct occurs. The U.K. Bribery Act applies to bribery activities both in the public and private sector and prohibits the provision of an "advantage" intended to induce or reward "improper performance" of the recipient's function. The failure by a company to prevent third parties from providing a bribe on its behalf could also constitute an offense. Penalties under the U.K. 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. Our clinical trial operations could also result in enforcement actions by U.S., U.K., or other governmental authorities. There are also trade laws within the United States and in other regions that regulate the sale, purchase, import, export, reexport, transfer and shipment of goods, currency, products, materials, services and technology. Violations of these laws can lead to serious consequences, including substantial fines.

The processing of personal data in the European Economic Area, consisting of the EU Member States plus Iceland, Liechtenstein and Norway, or the EEA, is subject to the 1995 Data Protection Directive, or the Directive, as implemented into the national laws of the EEA member states. The Directive imposes a number of strict obligations and restrictions on the ability to collect, analyze and transfer personal data, including health data collected during clinical trials and adverse event reporting. In May 2018, a new privacy regime, the General Data Protection Regulation, or GDPR, will take effect and immediately be binding across all EEA member states. The GDPR increases our obligations with respect to clinical trials conducted in the EEA by expanding the definition of personal data to include coded data, and requiring changes to informed consent practices and requiring more detailed notices be provided to clinical trial subjects and investigators. In addition, the GDPR increases the scrutiny that clinical trial sites located in the EEA should apply to transfers of personal data from such sites to countries that are considered by the European Commission to lack an adequate level of data protection, such as the United States. The compliance obligations imposed by the GDPR may increase our cost of doing business. In addition, the GDPR imposes substantial fines for breaches of data protection requirements, which can be up to four percent of global turnover or 20 million Euros, whichever is greater, and it also confers a private right of action on data subjects for breaches of data protection requirements.

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, 2017, we had 114 employees, 113 of whom were full-time, 27 of whom hold Ph.D. or M.D. degrees, 38 of whom were engaged in research and development activities and 46 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 3,384 square feet of that space. 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, Suite 1100, Cambridge, Massachusetts 02142. Our telephone number is (617) 871-2098. Our website address is www.akebia.com. The information on our website or that may be accessed by links on our website is not incorporated by reference into this Form 10-K. We make available, free of charge and through our 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

We face a variety of risks and uncertainties in our business. Additional risks and uncertainties not presently known to us or that we currently believe to be immaterial may also become important factors that affect our business. 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 net losses since inception and anticipate that we will continue to incur significant and increasing net losses for the foreseeable future.

Investment in pharmaceutical product development is highly speculative because it entails upfront capital expenditures and significant risk that a product candidate will fail to gain marketing approval or become commercially viable. Since our inception, we have devoted most of our resources to research and development, including our preclinical and clinical development activities. We have financed our operations primarily through sales of equity securities and our strategic collaborations. To date, we have no products approved for commercial sale and have not generated any revenue from the sale of products. As a result, we are not profitable and have incurred net losses each year since our inception, including net losses of $76.9 million for the year ended December 31, 2017. As of December 31, 2017, we had an accumulated deficit of $374.1 million. We do not know whether or when we will generate product revenue or become profitable.

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

- conduct our development program of vadadustat for the treatment of anemia due to chronic kidney disease, or CKD, including PRO$_2$TECT, INNO$_2$VATE, FO$_2$RWARD and TRILO$_2$GY, and develop plans for the preclinical and clinical development of any other potential product candidates;
- seek marketing approvals for our product candidates that successfully complete clinical studies, and maintain such marketing approvals, including complying with any post-marketing regulatory requirements;
- 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 vadadustat and any other product candidates;
- seek to discover and develop additional product candidates;
- engage in transactions, including strategic transactions, merger, collaboration, acquisition and licensing arrangements, pursuant to which we would market and develop commercial products, or develop other product candidates and technologies;
- make royalty, milestone or other payments under our license agreement with Janssen Pharmaceutica NV, or Janssen, and any future in-license agreements;
- maintain, protect and expand our intellectual property portfolio;
- attract and retain skilled personnel;
- continue to create additional infrastructure and expend additional resources to support our operations as a public company, including any additional infrastructure and resources necessary to support a transition from our status as an emerging grown company; and
- experience any delays or encounter issues with any of the above.

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. 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. In any particular quarter, the progress of our clinical development and our operating results could be below the expectations of securities analysts or investors, which could cause our stock price to decline.

Even if we succeed in receiving marketing approval for and are able to commercialize vadadustat, we will continue to incur substantial research and development and other expenditures to develop and market, if approved, any other product candidates as well as any costs relating to post-marketing requirements for vadadustat. Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital.

We have never generated any revenue from product sales, and we may never be profitable.

We have no products approved for commercial sale, have never generated any revenue from product sales, and do not anticipate generating any revenue from product sales until after we receive marketing approval for the commercial sale of a product candidate, if ever. Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict when, if at all, we will be able to achieve profitability. Our ability to generate revenue and achieve profitability depends significantly on our success in many factors, including the following:

- completing research regarding, and preclinical and clinical development of, our product candidates;
- seeking and obtaining marketing approvals for our product candidates for which we complete clinical studies and the timing of such approvals;
- developing sustainable and scalable manufacturing processes for our product candidates;
- establishing and maintaining supply and manufacturing relationships with third parties that can provide adequate products and services to support clinical development and the market demand for our product candidates, if approved;
- launching and commercializing our product candidates, either directly or with a collaborator or distributor;
- obtaining sufficient pricing and reimbursement for our product candidates from private and governmental payors;
- obtaining market acceptance of our product candidates as viable treatment options;
- the size of any market in which our product candidates receive approval and adequate market share in those markets;
- addressing any competing technological and market developments;
- identifying, assessing, acquiring and/or developing new product candidates;
- negotiating favorable terms in any transaction into which we may enter, including collaboration, merger, acquisition and licensing arrangements;
- maintaining, protecting and expanding our portfolio of intellectual property rights, including patents, trade secrets and know-how; and
- attracting, hiring and retaining qualified personnel.

Our expenses could increase beyond expectations if we are required by the U.S. Food and Drug Administration, or FDA, the European Medicines Agency, or EMA, or other regulatory authorities, or if we otherwise believe it is necessary, to change our manufacturing processes or assays, to amend or replace our study protocols, to repeat any of our clinical trials, or 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. Even if our product candidates are approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. In addition, our ability to generate revenue would be negatively affected if the size of our addressable patient population is not as significant as we estimate, the indication approved by regulatory authorities is narrower than we expect, or the patient population for treatment is narrowed by competition, physician choice, or payor or treatment guidelines. Even if we are able to generate revenues from the sale of any approved products, we may never generate revenue that is significant enough to become and remain profitable, and we may need to obtain additional funding to continue operations.

We will require substantial additional financing to achieve our goals. 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, 2017, our cash and cash equivalents and available for sale securities were $317.8 million. We expect to continue to expend substantial amounts for the foreseeable future developing and commercializing vadadustat, if approved, and any other product candidates. These expenditures will include costs associated with research and development, potentially obtaining marketing 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, including as a result of our decision to include certain elements in our development 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 global Phase 3 development program for vadadustat for the treatment of anemia due to CKD. As of December 31, 2017, we expect the remaining external aggregate contract research organization, or CRO, costs of PRO_2TECT and $INNO_2$VATE, which are designed to enroll up to 6,900 subjects, to be in the range of $420.0 million to $450.0 million; the estimated costs for PRO_2TECT and $INNO_2$VATE could increase significantly due to a number of factors, including changes in target enrollment and enrollment rates, the addition of new investigative sites, modification of clinical trial protocols, performing other studies in support of the Phase 3 program; choosing to add third-party vendors to support the program, and any other factor that could delay completion of PRO_2TECT and $INNO_2$VATE.
- the results of our meetings with the FDA, 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;
- the timing of, and the costs involved in, obtaining marketing approvals for vadadustat and any other product candidates that we may develop or acquire, if clinical studies are successful, including to fund the preparation and filing of regulatory submissions with the FDA, the EMA and other regulatory authorities;
- the cost of conducting the new FO_2RWARD and TRILO$_2$GY clinical studies;
- 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 vadadustat, as well as any studies of any other product candidates;
- the cost of securing and validating commercial manufacturing of vadadustat;
- the cost and timing of future commercialization activities for our products, if approved for marketing, including product manufacturing, marketing, sales and distribution costs;
- 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 engage in transactions, including collaboration, merger, acquisition and licensing arrangements pursuant to which we would market and develop commercial products, or develop other product candidates and technologies.

We expect our existing cash resources, including the timing of committed research and development funding from our collaborators, to fund our current operating plan into the second quarter of 2019. 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. Furthermore, our development milestones may not be achieved, we may not receive the anticipated funding from our collaboration partners, and we may not secure other sources of financing. 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 or debt offerings, payments from our collaborators, strategic transactions, or a combination of these approaches. Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or if we have specific strategic objectives.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. In addition, additional funds may not be available to us in sufficient amounts or on acceptable terms or at all. If we are unable to raise additional capital in sufficient amounts when needed 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. 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 public or private equity or debt offerings, payments from our collaborators, strategic transactions, or a combination of these approaches. 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, our fixed payment obligations may increase, any such securities may have rights senior to those of our common stock, 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 would restrict our operations and potentially impair our competitiveness, such as limitations on our ability to incur additional debt, make capital expenditures, declare dividends, acquire, sell or license intellectual property rights, and other operating restrictions that could adversely impact our ability to conduct our business. If we raise additional funds through strategic transactions with third parties, we may have to do so at an earlier stage than otherwise would be desirable. In connection with any such strategic transactions, we may be required 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, 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 and our Other Product Candidates

We depend heavily on the success of one product candidate, vadadustat, which is currently in Phase 3 development. Clinical drug development involves a lengthy and expensive process with an uncertain outcome. We will incur additional costs in connection with, and may experience delays in completing, or ultimately be unable to complete, the development and commercialization of vadadustat and any other product candidates.

The risk of failure in drug development is high. We currently have only one product candidate, vadadustat, in clinical development, and our business depends almost entirely on the successful clinical development, marketing approval and commercialization of vadadustat, which may never occur. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical trials are expensive, difficult to design and implement, can take several years to complete, and their outcomes are inherently uncertain. Failure can occur at any time during the clinical trial process. Further, the results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials, and interim results of a clinical trial do not necessarily predict final results. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their product candidates. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans or will receive marketing approval.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates. Our clinical trials may take longer to complete than currently anticipated, or may be delayed, suspended, required to be repeated or prematurely terminated because costs are greater than we anticipate or for a variety of other reasons, such as:

- the number of patients required for clinical trials of our product candidates may be larger than we anticipate;
- enrollment in our clinical trials may be slower than we anticipate, or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements, perform effectively, or meet their contractual obligations to us in a timely manner, or at all, or we may fail to communicate effectively or provide the appropriate level of oversight of such third-party contractors;
- the supply or quality of our starting materials, drug substance and drug product necessary to conduct clinical trials of our product candidates may be insufficient or inadequate;
- regulators, international data monitoring committees, or IDMCs, institutional review boards, or IRBs, safety committees, or ethics committees, may require that we suspend or terminate our clinical trials for various reasons, including noncompliance with regulatory requirements, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using our product candidate, or a finding that the participants are being exposed to unacceptable health risks;

- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials, repeat a clinical trial or abandon product development programs;
- lack of adequate funding to continue a clinical trial, including unforeseen costs due to enrollment delays, requirements to conduct additional clinical trials or repeat a clinical trial and increased expenses associated with the services of our CROs and other third parties;
- failure to initiate, delay of or failure to complete a clinical trial as a result of an Investigational New Drug Application, or IND, being placed on clinical hold by the FDA, EMA, the Japanese Pharmaceuticals and Medical Devices Agency, or PMDA, or other regulatory authorities, or for other reasons;
- clinical trial sites and investigators deviating from the clinical protocol, failing to conduct the trial in accordance with regulatory requirements, or dropping out of a trial, or failure by us or our CROs to communicate effectively or provide the appropriate level of oversight of such clinical sites and investigators;
- delay or failure in having subjects complete a clinical trial or return for post-treatment follow-up;
- delay or failure in recruiting and enrolling suitable subjects to participate in a clinical trial;
- inability, delay, or failure in identifying and maintaining a sufficient number of clinical trial sites, many of which may already be engaged in other clinical programs;
- delay or failure in reaching agreement with the FDA, EMA, PMDA or other regulatory authorities on a clinical trial design upon which we are able to execute;
- delay or failure in obtaining authorization to commence a clinical trial or inability to comply with conditions imposed by a regulatory authority regarding the scope or design of a clinical trial;
- delays in reaching, or failure to reach, agreement on acceptable terms with prospective clinical trial sites and prospective CROs, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;
- the FDA, EMA, PMDA or other regulatory authorities may require us to submit additional data or impose further requirements before permitting us to initiate a clinical trial;
- failure to comply with good practice quality guidelines and regulations, or GXP, including good laboratory practice, or GLP, good clinical practice, or GCP, and current good manufacturing practice, or cGMP; or
- changes in governmental regulations or administrative actions.

Many of the factors that cause or lead to a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of marketing approval for our product candidates. Further, the FDA, EMA, PMDA or other regulatory authorities may disagree with our clinical trial design and our interpretation of data from clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials.

If we are required to conduct additional clinical trials, repeat clinical trials or conduct other studies of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other studies, if the results of these trials or tests are not positive or are only modestly positive, or if there are safety concerns, we may:

- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval for our product candidates at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings that would reduce the potential market for our products or inhibit our ability to successfully commercialize our products;
- be subject to additional post-marketing restrictions and/or requirements; or
- have the product removed from the market after obtaining marketing approval.

Our product development costs will also increase if we experience delays in preclinical and clinical development or receiving the requisite marketing approvals. We do not know whether any of our preclinical studies or clinical trials will need to be restructured or will be completed on schedule, or at all. Significant preclinical or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do. This could impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

Even if we obtain favorable clinical results in our Phase 3 studies, we may not be able to obtain marketing approval for, or successfully commercialize, vadadustat, or we may experience significant delays in doing so, any of which would materially harm our business.

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, and in other countries where we and our collaborators intend to test and, if approved, market any product candidates. Before obtaining marketing 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 and in other jurisdictions, only a small percentage successfully complete the FDA and other jurisdictions' marketing approval processes and are commercialized. Accordingly, even if we are able to obtain the requisite capital to continue to fund our development programs, we may be unable to successfully develop or commercialize vadadustat or any other product candidates.

We and Otsuka Pharmaceutical Co. Ltd., or Otsuka, our collaboration partner, are not permitted to market vadadustat in the United States until we receive approval from the FDA, in the European Union until we receive approval from the EMA, or in any other jurisdiction until we receive the requisite approval from regulatory authorities in such jurisdiction. Mitsubishi Tanabe Pharma Corporation, or 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 marketing approval for vadadustat, we must complete Phase 3 studies and any additional preclinical or clinical studies required by the FDA, EMA, PMDA or other regulatory authorities. Vadadustat may not be successful in clinical trials or receive marketing approval. Further, vadadustat may not receive marketing approval even if it is successful in clinical trials.

Obtaining marketing approval in the United States and other jurisdictions is a complex, lengthy, expensive and uncertain process that typically takes many years and depends upon numerous factors, including the substantial discretion of the regulatory authorities. Even if our product candidates demonstrate safety and efficacy in clinical studies, the regulatory agencies may not complete their review processes in a timely manner, or we may not be able to obtain marketing approval. In addition, the safety concerns associated with injectable ESAs may affect the FDA's, EMA's, PMDA's or other regulatory authorities 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 marketing approval for any product candidate, and it is possible that vadadustat and any other product candidates will never obtain marketing approval. The FDA may delay, limit or deny approval of vadadustat or any other product candidates for many reasons including, among others:

- we may not be able to demonstrate that vadadustat is safe and effective in treating anemia due to CKD or that any other product candidate is safe and effective for its proposed indication(s) to the satisfaction of the FDA;
- the FDA may require us to complete both the INNO$_2$VATE clinical program and the PRO$_2$TECT clinical program for vadadustat prior to allowing us to file our NDA even if one of these programs finishes in advance of the other;
- 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 or any other product candidate;
- the FDA may approve vadadustat or any other product candidate for use only in a small patient population or for fewer or more limited indications than we request;
- the FDA may require that we conduct additional clinical trials or repeat one or more clinical trials;
- the FDA may grant approval contingent on the performance of costly post-marketing clinical trials;
- we, or our CROs or vendors, may fail to comply with GXP;
- the 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, or we may fail to communicate effectively or provide the appropriate level of oversight of our CROs;
- we or our third party manufacturers may fail to perform in accordance with the FDA's cGMP 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 preclinical studies and clinical trials;

the FDA could deem our financial relationships with principal investigators constitute a conflict of interest, such that the data from those principal investigators may not be used to support our applications;

an FDA Advisory Committee or other regulatory advisory group or authority could recommend non-approval or restrictions on approval;

the FDA's decision-making regarding vadadustat and any other product candidates may be impacted by the results of competitors' 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 or any other product candidate outside the United States.

If we experience delays in obtaining approval, or if we fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be materially impaired, which could have a material adverse effect on our business.

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 of vadadustat because of concerns about adverse events observed with injectable ESAs, 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 ESAs 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 and any other product candidates. As a result, the timeline for recruiting patients, conducting studies and obtaining marketing approval of vadadustat and any other product candidates may be delayed. These delays could result in increased costs, delays in advancing our development of vadadustat and any other product candidates, 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, including as a result of adverse effects observed in similar or competing therapies;

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 the product candidate being studied in relation to available therapies or other product candidates 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 could have a material 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 marketing approval of vadadustat for the treatment of anemia due 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 jurisdictions outside the United States, including:

difficulty in establishing or managing relationships with qualified CROs, physicians and clinical trial sites;

different local standards for the conduct of clinical studies;

difficulty in complying with various and complex import laws and regulations when shipping drug to certain countries; 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, PMDA 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. For example, in Japan, MTPC is conducting a Phase 3 program of vadadustat, which is separate from our global Phase 3 program of vadadustat.

If we have difficulty conducting our clinical studies in jurisdictions outside the United States as planned, we may need to delay, limit or terminate ongoing or planned clinical studies, any of which could have a material adverse effect on our business.

We may be delayed in obtaining, or be unable to obtain, marketing approval or reimbursement for vadadustat or any other product candidate in certain 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 marketed or sold in that country. In some cases, the prices that we intend to charge for our products are also subject to approval. Approval by the FDA does not ensure approval by regulatory or reimbursement authorities outside the United States, and approval by one regulatory or reimbursement authority outside the United States does not ensure approval by the FDA or any other regulatory or reimbursement authorities. However, the failure to obtain approval or reimbursement in one jurisdiction may negatively impact our ability to obtain approval or reimbursement in another jurisdiction. The marketing 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 or reimbursement approvals on a timely basis, if at all. We may not be able to file for marketing 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 or our control.

Positive results from preclinical and clinical studies are not necessarily predictive of the results of any future clinical studies. Furthermore, initial success in our ongoing clinical studies may not be indicative of results obtained when these studies are completed.

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, successful results from early or small clinical trials may not be replicated in later and larger clinical trials, and successful interim results from ongoing clinical studies may not be indicative of results obtained when those studies are completed. 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 global Phase 3 development program for vadadustat is enrolling 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 or any other product candidates 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 or any other product candidates.

We may not be successful in our efforts to identify, acquire, discover, develop and commercialize additional products or product candidates, which could impair our ability to grow.

Although we continue to focus a substantial amount of our efforts on the development and potential commercialization of vadadustat, a key element of our long-term growth strategy is to acquire, develop and/or market additional products and product candidates. Research programs to identify product candidates require substantial technical, financial and human resources, regardless of whether product candidates are ultimately identified. Our research and development programs may initially show promise, yet fail to yield product candidates for clinical development or commercialization for many reasons, including the following:

- the research methodology used may not be successful in identifying potential indications and/or product candidates;
- we may not be able or willing to assemble sufficient resources to acquire or discover additional product candidates;
- a product candidate may be shown to have harmful side effects or other characteristics that indicate it is unlikely to be effective or otherwise does not meet applicable regulatory criteria;
- product candidates we develop may nevertheless be covered by third-party patents or other exclusive rights;
- the market for a product candidate may change during our program so that the continued development of that product candidate is no longer reasonable;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; or
- a product candidate may not be accepted as safe and effective by patients, the medical community, or third-party payors, if applicable.

If any of these events occur, we may be forced to abandon our development efforts for one or more of our programs, or we may not be able to identify, discover, develop or commercialize additional product candidates, which would have a material adverse effect on our business.

Because we have limited financial and managerial resources, we focus on research programs and product candidates for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential or a greater likelihood of success. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities.

Because our internal research capabilities are limited, we may be dependent upon other pharmaceutical and biotechnology companies, academic scientists, and other researchers to sell or license products or technology to us. The success of this strategy depends partly upon our ability to identify, select, and acquire promising product candidates and products. The process of proposing, negotiating and implementing a license or acquisition of a product candidate or an approved product is lengthy and complex. Other companies, including some with substantially greater financial, marketing and sales resources, may compete with us for the license or acquisition of a product candidate or an approved product. We have limited resources to identify and execute the acquisition or in-licensing of third-party products, businesses, and technologies and integrate them into our current infrastructure.

Moreover, we may devote resources to potential acquisitions or in-licensing opportunities that are never completed, or we may fail to realize the anticipated benefits of such efforts. Any product candidate that we acquire may require additional development efforts prior to commercial sale, including extensive clinical testing and approval by the FDA, EMA, PMDA or other regulatory authorities. All product candidates are prone to risks of failure typical of pharmaceutical product development, including the possibility that a product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities. In addition, we cannot provide assurance that any products that we develop or approved products that we acquire will be manufactured profitably, achieve market acceptance or not require substantial post-marketing clinical trials.

Accordingly, there can be no assurance that we will ever be able to identify additional therapeutic opportunities for our product candidates or to acquire or develop suitable potential product candidates or approved products, which could materially adversely affect our future growth and prospects. We may focus our efforts and resources on potential product candidates or other programs that ultimately prove to be unsuccessful.

Our product candidates may cause undesirable side effects or have other properties that delay or prevent their marketing approval or limit their commercial potential.

Undesirable side effects caused by our product candidates or competing products in development that utilize a common mechanism of action could cause us or regulatory authorities to interrupt, delay or halt clinical trials, could result in a more restrictive label or the delay or the denial of marketing approval by the FDA or other regulatory authorities, and could lead to potential product liability claims. Results of our trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics.

The subjects 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 subjects 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 and any other product candidates could have a material adverse effect on the development of such 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 marketing approval for our product candidates or regulatory authorities may withdraw approvals of product candidates;
- regulatory authorities may require additional warnings on the label;
- Risk Evaluation and Mitigation Strategies, or REMS, FDA-imposed risk management plans that use risk minimization strategies to ensure that the benefits of certain prescription drugs outweigh their risks, 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 marketing approval and, ultimately, market acceptance of our products, could substantially increase our costs, and could significantly impact our ability to successfully commercialize our product candidates and generate revenues.

Any product candidate for which we obtain marketing approval will be subject to extensive post-marketing regulatory requirements and could be subject to post-marketing restrictions or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, when and if any of them is approved.

Any marketing 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, including REMS or registry or observational studies. In addition, if the FDA or any other regulatory authority 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 cGMPs and GCPs for any clinical trials that we conduct post-approval.

Moreover, the FDA and other regulatory authorities closely regulate the post-approval marketing and promotion of drugs to ensure drugs are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and other regulatory authorities impose stringent restrictions on companies' communications regarding use of their products, and if we promote our products beyond their approved indications or inconsistent with the approved label, we may be subject to enforcement actions or prosecution arising from such activities. Violations of the U.S. Federal Food, Drug, and Cosmetic Act, or the FD&C Act relating to the promotion of prescription drugs may lead to investigations alleging violations of U.S. federal and state healthcare fraud and abuse and other laws, as well as state consumer protection laws, third party payor actions, shareholder actions and other lawsuits.

Post-approval discovery of previously unknown problems with an approved 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, distribution, use or manufacturing of the product;
- withdrawal of the product from the market, or product recalls;
- restrictions on the labeling or marketing of a product;
- fines, restitution or disgorgement of profits or revenues;
- warning or untitled 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;
- REMS; and
- injunctions or the imposition of civil or criminal penalties.

Non-compliance with FDA, EMA, PMDA and other regulatory authorities' requirements regarding safety monitoring or pharmacovigilance can also result in significant financial penalties.

The FDA's policies and those of other regulatory authorities 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 in other jurisdictions. 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 materially 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 successfully carry out their contractual duties, comply with regulatory requirements or meet expected deadlines, we may not be able to obtain marketing approval for or commercialize vadadustat or any other product candidates, and our business could be substantially harmed.

We do not have the ability to independently conduct preclinical and clinical trials. 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 preclinical studies and our clinical trials, including our global Phase 3 development program for vadadustat. The third parties on whom we rely may fail to perform effectively or terminate their engagement with us for a number of reasons, including the following:

- if the quantity or accuracy of the data obtained by the third parties is compromised due to their failure to adhere to clinical trial protocols or to regulatory requirements, or if the third parties otherwise fail to comply with clinical trial protocols, perform effectively or meet expected deadlines;
- if third parties experience staffing difficulties;
- if we fail to communicate effectively or provide the appropriate level of oversight;
- if third parties undergo changes in priorities or corporate structure or become financially distressed; or
- if they form relationships with other entities, some of which may be our competitors.

Any of these events could cause our preclinical and clinical trials to be extended, delayed, suspended, required to be repeated or terminated, or we may receive untitled warning letters or be the subject of an enforcement action which could result in our failing to obtain marketing approval of vadadustat or any other product candidates on a timely basis, or at all, and would adversely affect our business operations. In addition, if the third parties on whom we rely may fail to perform effectively or terminate their engagement with us, we may need to enter into alternative arrangements, which could delay, perhaps significantly, development and commercialization of vadadustat and any other product candidates.

Even though we do not directly control the third parties on whom we rely to conduct our preclinical and clinical trials and therefore cannot guarantee the satisfactory and timely performance of their obligations to us, we are nevertheless responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol, legal and regulatory requirements, including GXP requirements, and scientific standards, and our reliance on these third parties, including CROs, will not relieve us of our regulatory

responsibilities. If we or any of our CROs, their subcontractors, or clinical trial sites fail to comply with applicable GXP requirements, the clinical data generated in our clinical trials may be deemed unreliable or insufficient, and the FDA, EMA or other regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. In addition, our clinical trials must be conducted with drug product that meets certain specifications and is manufactured under applicable cGMP regulations. These requirements include, among other things, quality control, quality assurance, and the satisfactory maintenance of records and documentation.

We also 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 costs and depriving us of potential product revenue. In addition, we are using an active comparator in our PRO_2TECT and $INNO_2VATE$ clinical programs. 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 all aspects of our product manufacturing. If they do not successfully carry out their contractual duties, comply with regulatory requirements or meet expected deadlines, we may not be able to obtain marketing approval for or commercialize vadadustat or any other product candidates, and our business could be substantially harmed.

We do not have any manufacturing facilities and do not expect to independently manufacture our product candidates for research and preclinical and clinical studies or, if our product candidates are approved, for commercial purposes. We currently rely on third party manufacturers to produce all of our preclinical and clinical material supply. We expect to continue to rely on existing or alternative third party manufacturers to supply our ongoing and planned preclinical and clinical trials and for commercial production. We have not yet entered into binding agreements with third party manufacturers to manufacture commercial quantities of vadadustat, and we may not be able to negotiate binding agreements at commercially reasonable terms. Our reliance on third party manufacturers increases the risk that we will not have sufficient quantities of our product candidates or the ability to obtain such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

If any of our third-party manufacturers cannot perform as agreed, including a misappropriation of our proprietary information, or if they terminate their engagements with us, we may be forced to manufacture the materials ourselves, for which we currently do not have the capabilities or resources, or enter into agreements with other third party manufacturers, which we may not be able to do on favorable or reasonable terms, if at all. In some cases, there may be a limited number of qualified replacement manufacturers, or the technical skills or technology required to manufacture a product candidate may be unique or proprietary to the original manufacturer and we may have difficulty transferring such skills or technology to another third party or a feasible alternative may not exist. These factors would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to have another third party manufacture our product candidates. If we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines. The delays associated with the verification of a new manufacturer could negatively affect our ability to develop and receive marketing approval for product candidates in a timely manner or within budget or, if vadadustat or any other product candidate is approved and marketed, a failure to satisfy patient demand.

The facilities and processes used by our third party manufacturers to manufacture our product candidates will be inspected by the FDA, EMA and other regulatory authorities prior to or after we submit our marketing application. We do not control the manufacturing processes of, and are completely dependent on, our third party manufacturers for compliance with cGMP requirements for manufacture of certain starting materials, drug substance and finished drug product. If our third party manufacturers cannot successfully manufacture material that conforms to our specifications and regulatory requirements, we will not be able to secure and/or maintain marketing approval for our product candidates. In addition, we have no control over the ability of our third party 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 marketing approval for or market our product candidates, if approved. Moreover, the failure of our third party 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, if approved, operating restrictions or criminal prosecutions, any of which could significantly and adversely affect the supply of our product candidates or products, if approved. Also, if our starting materials, drug substance or drug product are damaged or lost while in our third party manufacturers' control, it may impact our ability to supply our products, if approved, or product candidates and we may incur significant financial harm. In addition, our product candidates and products, if approved, may compete with other product candidates and products for access to third party manufacturing facilities. Certain of these third party manufacturing facilities may be contractually prohibited from manufacturing our product candidates or products, if approved, 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 our product candidates and product, if approved, for us.

Our current and anticipated future dependence on third parties for the manufacture of our product candidates or our products, if approved, may adversely affect our ability to commercialize any drugs that receive marketing approval on a timely and competitive basis and any future profit margins.

If we are unable to obtain our product candidates or products, if approved, in sufficient quantities and at sufficient yields, we may experience delays in product development, preclinical or clinical studies, marketing approvals and commercial distribution.

Completion of our preclinical and clinical studies 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 managing third parties in manufacturing our product candidates or products, if approved, in the volumes that will be necessary to support large-scale clinical trials or commercial sales. Our third party manufacturers may not meet our expectations as to scheduling, scale-up, reproducibility, yield, purity, cost, potency or quality.

Our reliance on third party 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 third party manufacturers with the expertise, required marketing approvals and facilities to manufacture our bulk starting materials, drug substance and finished drug product on a commercial scale, replacement of a third party manufacturer may be expensive and time-consuming and may cause interruptions in the production of our product candidates or products, if approved. A third party manufacturer may also encounter delays brought on by sudden internal resource constraints, labor disputes, or shifting regulatory protocols. In addition, a contract manufacturer may also require a substantial financial commitment, including but not limited to a commitment to fund the purchase of a new facility or equipment.

Any delay or interruption in our supply of product candidates or products, if approved, could cause delays in our product development, clinical trials, marketing approvals, commercial distribution, or have a material adverse effect on our business, financial condition, results of operations and cash flows.

Third party manufacturers may be unable to successfully scale-up manufacturing of our product candidates in sufficient quality and quantity, which would delay or prevent us from developing our product candidates and commercializing approved products, if any.

In order to complete our development of and commercialize, if approved, vadadustat and any other product candidates, we will need to work with third party manufacturers to manufacture them in large quantities. Our current and future third party manufacturers may be unable to successfully achieve commercial scale production of vadadustat or increase the manufacturing capacity of any other product candidates for the conduct of clinical trials and commercialization in a timely or cost-effective manner, if at all. In addition, quality issues may arise during scale-up activities. Any changes in our manufacturing processes as a result of scaling up may result in the need to obtain additional marketing approvals. If our third party manufacturers are unable to achieve commercial scale production or there is a need for additional marketing approvals of vadadustat or any other product candidates, or if there are difficulties in increasing the manufacturing capacity for any other product candidates, the development, marketing approval and commercialization of that product candidate may be delayed or infeasible, or ongoing commercialization may be unsuccessful, any of which could significantly harm our business.

The loss of any of our manufacturers could materially harm our business.

We currently have redundant supply arrangements in place for the preclinical and clinical supply of vadadustat. We have not yet entered into binding agreements with third party manufacturers to manufacture commercial quantities of vadadustat. While we intend to put redundant supply arrangements in place for commercial manufacturing of vadadustat, we may be unsuccessful in doing so due to a number of factors, including that we may not be able to negotiate binding agreements at commercially reasonable terms. Even if we are ultimately successful in entering into redundant supply arrangements for commercial manufacturing of vadadustat, the timing of such arrangements is uncertain and may occur following the launch of vadadustat, if approved for marketing. The drug substance and drug product for AKB-5169 are supplied to us from single source suppliers with limited capacity.

We do not know whether our third party manufacturers will be able to meet our demand, either because of the nature of our agreements with those third party manufacturers, our limited experience with those third party manufacturers or our relative importance as a customer to those third party manufacturers. It may be difficult for us to assess their ability to timely meet our demand in the future based on past performance. While our current third party manufacturers have generally met our demand for their products on a timely basis in the past, they may subordinate our needs in the future to their other customers.

If we are unsuccessful in implementing redundant supply arrangements for commercial quantities of vadadustat, or if any of our third party manufacturers are unable to fulfill the terms of their agreements with us, are subject to regulatory review, or cease their

operations for any reason, it could result in delays to our marketing approval and risk that we would not have sufficient quantities of our product candidates, and if approved, products, for clinical trials and commercialization.

We depend on our collaborations with Otsuka and MTPC for the development and commercialization of vadadustat, and we may depend on collaborations with additional third parties for the development and commercialization of vadadustat and any other product candidates. If our collaborations are not successful or if our collaborators terminate their agreements with us, we may not be able to capitalize on the market potential of vadadustat or any other product candidates and our business could be materially harmed.

We entered into collaboration agreements with Otsuka to develop and commercialize vadadustat in the United States, Europe, China and certain other territories. We also entered into a collaboration agreement with MTPC to develop and commercialize vadadustat in Japan and certain other Asian countries. We may form or seek other strategic alliances, joint ventures, or collaborations, or enter into additional licensing arrangements with third parties that we believe will complement or augment our development and commercialization efforts with respect to vadadustat and any other product candidates. Our likely collaborators for any collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies.

We may not be able to maintain our collaborations and our collaborations may not be successful due to a number of important factors, including the following:

- collaborators may have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborations may be terminated in accordance with the terms of the collaborations and, if terminated, may make it difficult for us to attract new collaborators or adversely affect how we are perceived in scientific and financial communities, and may result in a need for additional capital and expansion of our internal capabilities to pursue further development or commercialization of the applicable product candidates;
- if permitted by the terms of the collaborations, collaborators may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in their strategic focus, availability of funding or other external factors such as a business combination that diverts resources or creates competing priorities;
- if permitted by the terms of the collaborations, collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial, abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to their marketing and distribution;
- if permitted by the terms of the collaboration, we and our collaborator may have a difference of opinion regarding the commercialization strategy for a particular product, and our collaborator may have ultimate decision making authority;
- disputes may arise between a collaborator and us that cause the delay or termination activities related to research, development or commercialization of vadadustat and any other product candidates, or that result in costly litigation or arbitration that diverts management attention and resources;
- collaborations may not lead to development or commercialization of product candidates in the most efficient manner or at all;
- a significant change in the senior management team, a change in the financial condition or a change in the business operations, including a change in control or internal corporate restructuring, of any of our collaborators, could result in delayed timelines, re-prioritization of our programs, decreasing resources or funding allocated to support our programs, or termination of the collaborations; and
- collaborators may not comply with all applicable regulatory requirements.

If any of these events occur, the market potential of our product candidates could be reduced, and our business could be materially harmed. We also cannot be certain that, following a collaboration, we will achieve the revenue or specific net income that justifies such transaction.

We may seek to establish additional collaborations and, if we are not able to establish them on commercially reasonable terms, we may have to alter our development and commercialization plans.

We will require substantial additional cash to fund the development and potential commercialization of vadadustat and any other product candidates. For some of our product candidates, including vadadustat, we may decide to enter into additional collaborations for their development and potential commercialization. Any of these relationships may require us to incur non-recurring and other charges, increase our near and long-term expenditures, issue securities that dilute our existing stockholders, or disrupt our management and business.

We may not be successful in entering into additional collaborations as a result of many factors including the following:

- competition in seeking appropriate collaborators;
- a reduced number of potential collaborators due to recent business combinations in the pharmaceutical industry;
- inability to negotiate collaborations on acceptable terms;
- inability to negotiate collaborations on a timely basis;
- a potential collaborator's evaluation of our product candidate;
- a potential collaborator's resources and expertise; and
- restrictions due to an existing collaboration agreement.

If we are unable to enter into additional collaborations, we may have to curtail the development of the product candidate on which we are seeking to collaborate, reduce or delay its development program or other of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

Even if we enter into additional collaboration agreements and strategic partnerships or license our intellectual property, we may not be able to maintain them or they may be unsuccessful, which could delay our timelines or otherwise adversely affect our business.

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 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 our issued European patents, European Patent No. 2044005, or the '005 EP 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 appealed the decision of the Opposition Division. On February 27, 2018, we withdrew the '005 EP Patent from appeal and filed a divisional patent application to pursue a focused claim set that includes claims for vadadustat, as well as pharmaceutical compositions and methods of treating anemia. We cannot be assured that such claims in the divisional application will be granted by the European Patent Office. If such claims are not granted, or the scope of the claims is significantly narrowed, we may not be able to adequately protect our rights, provide sufficient exclusivity, or preserve our competitive advantage.

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 taken, 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 of these patents, such actions 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. 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 of 2011, which brought into effect significant changes to the U.S. patent laws and introduced new procedures for challenging pending patent applications and issued patents. A primary change under this reform was creating a "first to file" system in the United States. This requires 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 processes, and any other elements of our drug discovery and development process and information or technology that are 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, collaborators 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 assist with research, development and manufacture of 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, collaborators 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 information becomes known by our competitors, is inadvertently incorporated into the technology of others, or is 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 with which we may collaborate 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 disclosure or publication of information by any of our employees, advisors, consultants, third party contractors or 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 agreements could jeopardize our rights in such product candidates and materially harm our business.

We license intellectual property rights from third parties that protect some of our product candidates. 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, development and commercialization 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 will prevent us from commercializing vadadustat; 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 due 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 discuss the status of the opposition proceedings against FibroGen's European '823, '153,'155 and '333 EP Patents below in Part I, 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 or any other product candidates. 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.

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. 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.

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. An unfavorable outcome in any current or future proceeding in which we are challenging third party patents could require us to cease using the patented 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.

For example, we are currently involved in four 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 Our Intellectual Property" and Part I, Item 3 – Legal Proceedings.

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 governmental patent agencies in other jurisdictions 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 in many cases can 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 product 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. As a result, 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, impact our regulatory filings, or compromise our ability to protect our intellectual property.

A security breach, cyber-attack or unauthorized access of our clinical data or other data could damage the integrity of our clinical trial data, impact our regulatory filings, cause significant risk to our business, and 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, such as our CROs, 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 or any other product candidates, these product candidates may not gain market acceptance among physicians, patients, third-party payors, and others in the medical community in the United States or in other countries. In addition, market acceptance of any approved product 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 countries in which marketing approvals are obtained;
- the claims we and our collaborators are able to make regarding the safety and efficacy of our products;
- the success of our physician and patient communications and education programs;
- 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 receipt of marketing approvals and product launch relative to competing products and potential generic entrants;
- the availability of adequate coverage and reimbursement by third-party payors and governmental authorities, including patient cost-sharing programs such as copays and deductibles;
- relative convenience and ease of administration;
- the prevalence and severity of adverse side effects;
- adverse publicity about our products or favorable publicity about competing products;
- the effectiveness of our and our collaborators' sales, marketing and distribution 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. If vadadustat is approved and included in the fixed reimbursement model for a bundle of dialysis services, or the bundle, we would be required to enter into contracts to supply vadadustat to specific dialysis clinics, instead of through third party payors, which we believe could be challenging. In May 2017, we entered into a license agreement pursuant to which we will grant Vifor (International) Ltd., or Vifor Pharma, an exclusive license to sell vadadustat solely to Fresenius Kidney Care Group LLC, or FKC, in the United States; however, FKC is not obligated to utilize vadadustat in its clinics. Moreover, even if FKC chooses to utilize in vadadustat its clinics in the United States, it is not restricted from utilizing other therapies for anemia due to CKD. The Vifor Agreement does not restrict us from entering into supply agreements with other dialysis clinics, such as DaVita, one of the largest operators of dialysis clinical in the United States; however, the dialysis clinics may not choose to contract with us for vadadustat or they may choose to contract with us

for a limited supply of vadadustat. Although we currently believe it likely that vadadustat will be included in the bundle, if vadadustat is not included in the bundle, then the Vifor Agreement will not become effective, and patients would access vadadustat via contracts we negotiate with third party payors for reimbursement of vadadustat, which would be subject to the risks and uncertainties described above.

Market acceptance is critical to our ability to generate significant revenue. In addition, any product candidate, if approved and commercialized, may achieve only limited market acceptance or none at all. If any of our 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.

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 they are approved.

We are currently collaborating with Otsuka to develop and commercialize vadadustat in the United States, Europe, China and certain other jurisdictions and with MTPC to develop and commercialize vadadustat in Japan and certain other Asian countries. We do not have a sales or marketing infrastructure and we have not yet sold, marketed or distributed any 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, including the following:

- potential inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- potential inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe our products, if approved;
- potential lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- costs and expenses associated with creating an independent sales and marketing organization.

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 for the United States and Latin America and, as a result, we must 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 will be dependent on Otsuka, MTPC and any future commercialization partners to commercialize vadadustat. If Otsuka, MTPC or any future commercialization partner fails to perform under our agreements, our future results could be materially harmed.

We and Otsuka share the obligations to commercialize vadadustat in the United States; however, we are dependent on Otsuka to commercialize vadadustat in Europe, China and certain other territories and on MTPC to commercialize vadadustat in Japan and certain other Asian countries. If either of these collaborators fails to perform their obligations diligently under their agreements with us, including failing to diligently commercialize vadadustat in their territories, our sales potential in these regions 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 us 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, as well as 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. In the United States, there are multiple government and private third party payors with varying coverage and reimbursement levels for pharmaceutical products. Within Medicare, for oral drugs dispensed by pharmacies and also administered in facilities, coverage and reimbursement may vary depending on the setting. The Centers for Medicare & Medicaid Services, or CMS, local Medicare administrative contractors and/or Medicare Part D plans may have some responsibility for determining the medical necessity of such drugs, and therefore coverage, for different patients. Different reimbursement methodologies may apply and CMS may have some discretion in interpreting their application in certain settings. Medicaid reimbursement of drugs will also vary by state. Private third party payor reimbursement policies may also vary and may or may not be consistent with Medicare reimbursement methodologies. Manufacturers of outpatient prescription drugs may be required to provide discounts or rebates under government healthcare programs or to certain government or private purchasers in order to obtain coverage of such products under federal healthcare programs such as Medicaid.

Additionally, we may be required to enter into contracts with third-party payors offering rebates or discounts 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 for many reasons, including that we may be at a competitive disadvantage relative to companies with more extensive product lines. We cannot be sure that coverage or adequate reimbursement will be available for any of our product candidates. Even if we obtain coverage for any approved product, 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 is 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 reimbursement levels for 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 downward pressure on the pricing of drugs.

In addition, if vadadustat is approved and we are successful in entering into contracts to supply vadadustat to dialysis clinics, such facilities often receive fixed reimbursement for services, drugs and supplies included in the bundle. 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 CMS significantly reduces the level of reimbursement for dialysis services and providers choose to use alternative therapies or look to negotiate their contracts with us. Our profitability may also be affected 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 marketing approval.

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

In some countries, including 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 a significant amount of 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 or our collaborators 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, the commercial launch of our product candidate could be delayed, possibly for lengthy periods of time, we or our collaborators may not launch at all in a particular country, we may not be able to recoup our investment in one or more product candidates, and there could be a material adverse effect on our business.

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

Our revenue prospects could be affected by changes in healthcare spending and policy in the United States, Europe, China, Japan and other countries. We operate in a highly regulated industry and new laws, regulations or judicial decisions, or new interpretations of existing laws, regulations or decisions related to healthcare availability or the method of delivery or payment for healthcare products and services could negatively impact our business, operations and financial condition.

The United States federal and state governments continue to propose and pass legislation intended to reduce the cost of healthcare. One of these reforms was the Healthcare Reform Act, which included changes to the coverage and reimbursement of drugs under government healthcare programs, imposed new taxes on manufacturers of branded drugs, expanded health care coverage through Medicaid expansion, and implemented the individual health insurance mandate. Under the current administration, there have been ongoing efforts to modify or repeal all or certain provisions of the Health Care Reform Act. For instance, tax reform legislation was enacted at the end of 2017 that eliminated the individual health insurance mandate which is expected to increase the number of Americans without comprehensive health insurance. We cannot predict the ultimate content, timing or effect of any changes to the Healthcare Reform Act, and significant changes to, or repeal of, the Healthcare Reform Act could have a material adverse effect on our business, financial condition and profitability.

Additional legislative actions to control U.S. healthcare costs include the Budget Control Act, which imposed 2% reductions in Medicare payments to providers beginning in 2013. Subsequent legislation extended these reductions through 2025. Any significant spending reductions affecting Medicare, Medicaid or other publicly funded or subsidized health programs that may be implemented, or any significant taxes or fees that may be imposed on us, as part of any broader deficit reduction effort or legislative replacement to the Budget Control Act, could have an adverse impact on potential revenues we may receive from any approved products.

It is likely that federal and state legislatures within the United States and foreign governments will continue to consider changes to existing healthcare legislation. We cannot predict the reform initiatives that may be adopted in the future or whether initiatives that have been adopted will be repealed or modified. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare may adversely affect:

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

In the United States there is increasing scrutiny of drug prices and federal or state reforms could impact our ability to establish what we believe is a fair price for our product candidates upon approval, and ultimately diminish our revenue prospects.

Recently, there has been considerable public and government scrutiny in the United States of pharmaceutical pricing and proposals to address the perceived high cost of pharmaceuticals. There have also been several recent state legislative efforts to address drug costs, which generally have focused on increasing transparency around drug costs or limiting drug prices or price increases. Adoption of new legislation at the federal or state level could affect demand for, or pricing of, our product candidates, if approved, and could diminish our ability to establish what we believe is a fair price for our products, ultimately diminishing our revenue for our products if they approved.

Even prior to approval of any of our product candidates, we are subject to a complex regulatory scheme that requires significant resources to ensure compliance. Failure to comply with applicable laws could subject us 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 obtain approval for vadadustat or any other product candidate, certain laws apply to us or may otherwise restrict our activities, including the following:

- laws and regulations governing the conduct of preclinical and clinical studies in the United States and other 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 and regulations of countries outside the United States that prohibit pharmaceutical companies from promoting prescription drugs to the general public;

laws, regulations and industry codes that vary from country to country and govern our relationships with health care providers, patients, patient organizations, and other constituencies, prohibit certain types of gifts and entertainment, establish codes of conduct and, in some instances, require disclosure to, or approval by, regulatory authorities for us to engage in arrangements with such constituencies;

anti-corruption and anti-bribery laws, including the Foreign Corrupt Practices Act, or FCPA, the U.K. Bribery Act and various other anti-corruption laws in countries outside of the United States.

data privacy laws existing in the European Union and other countries in which we operate, including the U.S. Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and state privacy and data protection laws, as well as state consumer protection laws;

U.S. federal securities laws restricting the purchase or sale of any securities while in possession of material, non-public information; 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.

Compliance with these and other applicable laws and regulations requires us to expend significant resources. Failure to comply with these laws and regulations may subject us to penalties, damages, fines, the restructuring of our operations, or the imposition of a clinical hold, any of which could materially adversely affect our business and would result in increased costs and diversion of management attention.

Europe has enacted a new data privacy regulation, the General Data Protection Regulation, a violation of which could subject us to significant fines.

In May 2018, a new privacy regime, the General Data Protection Regulation, or GDPR, will take effect and immediately be binding across all member states of the European Economic Area, or EEA. The GDPR increases our obligations with respect to clinical trials conducted in the EEA by expanding the definition of personal data to include coded data, and requiring changes to informed consent practices and more detailed notices for clinical trial subjects and investigators. In addition, the GDPR increases the scrutiny that clinical trial sites located in the EEA should apply to transfers of personal data from such sites to countries that are considered to lack an adequate level of data protection, such as the United States. The GDPR imposes substantial fines for breaches of data protection requirements, which can be up to four percent of global turnover or 20 million Euros, whichever is greater, and it also confers a private right of action on data subjects for breaches of data protection requirements. Compliance with these directives will be a rigorous and time-intensive process that may increase our cost of doing business, and the failure to comply with these laws could subject us to significant fines.

If our product candidates obtain marketing approval, we will be subject to additional 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 U.S. federal government, states and governments outside of the United States in which we conduct our business. In addition to the laws mentioned above, the U.S. laws, and their non-U.S. equivalents, that may affect our ability to operate include:

the FD&C Act, which among other things, strictly regulates drug product marketing and promotion and prohibits manufacturers from marketing such products for off-label use;

the U.S. federal anti-kickback law, which prohibits, among other things, persons from soliciting, receiving or providing remuneration, directly or indirectly, to induce the referral for an item or service or the purchasing or ordering of a good or service for which payment may be made under U.S. federal healthcare programs such as Medicare and Medicaid;

U.S. 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 payors that are false or fraudulent;

U.S. 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 government healthcare programs;

the so-called "federal sunshine" law, in the U.S., which requires pharmaceutical and medical device manufacturers to report certain financial interactions to the federal government for re-disclosure to the public;

the U.S. federal law known as 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;

U.S. state law equivalents of the above U.S. federal laws, such as anti-kickback and false claims laws that may apply to items or services reimbursed by any third-party payor, including commercial insurers, and state gift ban and transparency laws, which are not preempted by federal laws and often differ from state to state, thus complicating compliance efforts; and

U.S. 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 U.S. laws, and their non-U.S. equivalents, 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 U.S. 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 healthcare programs in and out of the United States 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 drugs is highly competitive and subject to rapid and significant technological change. 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, any approved products that we commercialize will compete with existing, market-leading products.

If vadadustat is approved and launched commercially, competing drugs may include EPOGEN® (epoetin alfa) and Aranesp® (darbepoetin alfa), both commercialized by Amgen, Procrit® (epoetin alfa), Eprex® (epoetin alfa), commercialized by Johnson & Johnson, and Mircera® (methoxy PEG-epoetin beta), commercialized by Vifor Pharma in the United States and Roche Holding Ltd. outside the United States. In Europe and other markets, biosimilar versions of injectable ESAs are available and may become available in the United States in the future. We may also face competition from potential new anemia therapies. In addition, 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. Japan Tobacco International is currently in Phase 3 clinical development of its product candidate, JTZ-951, in Japan. GlaxoSmithKline plc has commenced Phase 3 studies of its product candidate, daprodustat, and Bayer HealthCare AG is currently in Phase 3 clinical development of its product candidate, molidustat, in Japan. Some of these product candidates may launch in certain markets as early as 2019. In addition, certain companies are developing potential new therapies for renal-related diseases that could potentially reduce injectable ESA utilization and thus limit the market potential for vadadustat if they are approved and launched commercially. Other new therapies are in development for the treatment of conditions inclusive of renal anemia that may impact the market for anemia-targeted treatment.

Because injectable ESAs are biologic products, the introduction of biosimilars into the injectable ESA 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 is a biologic product that is approved based on demonstrating that it is highly similar to an existing, FDA-approved branded biologic product. The patents for the existing, branded biologic 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 injectable ESA, expired in 2004 in the European Union, and the remaining patents expired between 2012 and 2016 in the United States. Several biosimilar versions of injectable ESAs are available for sale in the European Union and proposed biosimilar of injectable ESAs are currently in clinical development in the United States, including Pfizer and Vifor Pharma's proposed biosimilar of Retacrit® (epoetin alfa) which is currently under regulatory review at the FDA.

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 marketing 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 preclinical testing and clinical trials, obtaining marketing 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 candidates that we are developing obsolete. Smaller and other early stage companies may also prove to be significant competitors. As a result of all of these factors, our competitors may succeed in obtaining patent protection and/or marketing 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, keep and motivate senior management and key personnel, we may be unable to successfully develop and commercialize, if approved, our product candidates.

Recruiting and retaining qualified scientific, clinical, medical, manufacturing and sales and marketing personnel is critical to our success. We are also highly dependent on our executives and 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, senior managers 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 marketing 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 contractors, consultants and advisors, including scientific and clinical advisors, to assist us in formulating and executing our research and development and commercialization strategy. Our contractors, consultants and advisors may become employed by companies other than ours and may have commitments 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.

We are conducting global clinical trials in countries where corruption is prevalent. In addition, we are subject to a variety of import and export trade laws. Violations of any of these laws by our personnel or on the part of any of our vendors or agents, such as our CROs or CMOs, could have a material adverse impact on our clinical trials and our business and could result in criminal or civil fines and sanctions.

We are subject to complex laws that govern our international business practices. These laws include the FCPA, which prohibits U.S. companies and their intermediaries, such as CROs or CMOs, from making improper payments to foreign government officials for the purposes of obtaining or keeping business or to obtain any kind of advantage for the company. The FCPA also requires companies to keep accurate books and records and maintain adequate accounting controls. A number of past and recent FCPA investigations by the Department of Justice and the Securities and Exchange Commission have focused on the life sciences sector.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. Some of the countries in which we are conducting clinical trials have a history of corruption, which increases our risks of FCPA violations. In addition, the FCPA presents unique challenges in the pharmaceutical industry because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments made by pharmaceutical companies, or on their behalf by CROs, to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Additionally, the U.K. Bribery Act applies to our global activities. There are also local antibribery and anticorruption laws in countries where we are conducting clinical trials, and many of these also carry the risk of significant financial or criminal penalties.

We are also subject to trade control regulations and trade sanctions laws that restrict the movement of certain goods, currency, products, materials, services and technology to, and certain operations in, various countries or with certain persons. Our ability to transfer people and products among certain countries is subject to maintaining required licenses and complying with these laws and regulations.

The internal controls, policies and procedures, and training and compliance programs we have implemented to deter prohibited practices may not be effective in preventing our employees, contractors, consultants, agents or other representatives from violating or circumventing such internal policies or violating applicable laws and regulations. The failure to comply with laws governing international business practices may impact our clinical trials, result in substantial civil or criminal penalties for us and any such individuals, including imprisonment, suspension or debarment from government contracting, withdrawal of our products, if approved, from the market, or being delisted from The NASDAQ Global Market.

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 the following:

- 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;
- quality standards, including GXP;
- U.S. federal and state healthcare fraud and abuse laws and regulations and their non-U.S. equivalents;
- anti-bribery and anti-corruption laws, such as the FCPA and the U.K. Bribery Act or country-specific anti-bribery or anti-corruption laws, as well as various import and export laws and regulations;
- laws that require the reporting of true and accurate financial information and data; and
- U.S. securities laws and regulations and their non-U.S. equivalents.

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, disclosure of our confidential information 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, consultants, vendors, 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 qualified 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. If we 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, 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, contractors 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.

Our business and operations and our ability to protect our intellectual property may be materially adversely affected in the event of computer system failures or security breaches.

We deploy defenses against computer system failures and work to secure the integrity of our data systems using techniques, hardware and software typical of companies our size and scope. Despite the implementation of security measures, our internal computer systems, and those of our CROs and other third parties on which we rely, are vulnerable to damage from computer viruses, unauthorized access, and cyber attacks by increasingly sophisticated intruders or others who try to cause harm to or interfere with our normal use of our systems, as well as natural disasters, fire, terrorism, war and telecommunication and electrical failures. 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. If any of these events were to occur and cause interruptions in our operations, it could result in a material disruption of our drug development programs. For example, the loss of clinical trial data or other information from completed, ongoing or planned clinical trials could result in delays in our marketing approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur 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. 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 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 $1.07 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.

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 Ninth 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, 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. 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 Ninth 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 Ninth 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 Ninth 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 Ninth 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 Ninth 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.

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against companies for any of the reasons described in this section following a decline in the market price of their securities. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

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 currently sublease 3,384 square feet of that space. 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

Opposition Proceeding Against Our '005 EP Patent

In July 2011, a third party filed an opposition to our issued European Patent No. 2044005, or the '005 EP 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 appealed the decision of the Opposition Division. On February 27, 2018, we withdrew the '005 EP Patent from appeal and filed a divisional patent application to pursue a focused claim set that includes claims for vadadustat, as well as pharmaceutical compositions and methods of treating anemia. We cannot be assured that such claims in the divisional patent application will be granted by the European Patent Office. If such claims are not granted, or the scope of the claims is significantly narrowed, we may not be able to adequately protect our rights, provide sufficient exclusivity, or preserve our competitive advantage.

Opposition and Invalidity Proceedings Against FibroGen Inc.

We filed an opposition in Europe against FibroGen, Inc.'s, or FibroGen's, European Patent No. 1463823, or the '823 EP Patent, and 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 two to three 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 JP Patent, which is the Japanese counterpart to the '823 EP 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'131 JP 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 EP Patent and '131 JP Patents. In the event FibroGen were to obtain such a patent in the United States, we may decide to challenge the patent as 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. 2322155, or the '155 EP Patent, 1633333, or the '333 EP patent, and 2322153, or the '153 EP Patent requesting the patents be revoked in their entirety. These related patents claim, among other things, various compounds that either stabilize HIFα 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 our collaborators with maximum flexibility for developing vadadustat and our pipeline of HIF-PHIs.

Oppositions to the '155 EP Patent and the '153 EP Patent were also filed by Glaxo Group Limited, or Glaxo, and by Bayer Intellectual Property GmbH, Bayer Pharma Aktiengesellschaft, and Bayer Animal Health GmbH, or collectively Bayer.

With regards to the opposition that we filed in Europe against the '333 EP patent, an oral proceeding took place on 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. On December 9, 2016, FibroGen filed a notice to appeal the decision to revoke the '333 EP Patent.

In oral proceedings held on May 29, 2017, regarding the '155 EP Patent, the European Opposition Division ruled that the '155 EP Patent as granted did not meet the requirements for patentability under the European Patent Convention and, therefore, revoked the patent in its entirety. FibroGen filed a notice to appeal the decision to revoke the '155 EP Patent on May 29, 2017.

Subsequently, in related oral proceedings held on May 31, 2017 and June 1, 2017 for the '153 EP Patent, the European Opposition Division maintained the patent after FibroGen significantly narrowed the claims to an indication for which vadadustat is not intended to be developed. We and Glaxo separately filed notices to appeal the decision to maintain the '153 EP Patent on November 9, 2017. Bayer filed a notice to appeal the decision on November 14, 2017.

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
2017		
First Quarter	$ 10.70	$ 8.58
Second Quarter	$ 16.54	$ 8.69
Third Quarter	$ 19.73	$ 12.78
Fourth Quarter	$ 20.25	$ 14.07

	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

Holders

At March 1, 2018, there were approximately 22 holders of record of our common stock. The actual number of holders of our common stock is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers or held by other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividends

We have never declared or paid any cash dividends on our common stock. 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.

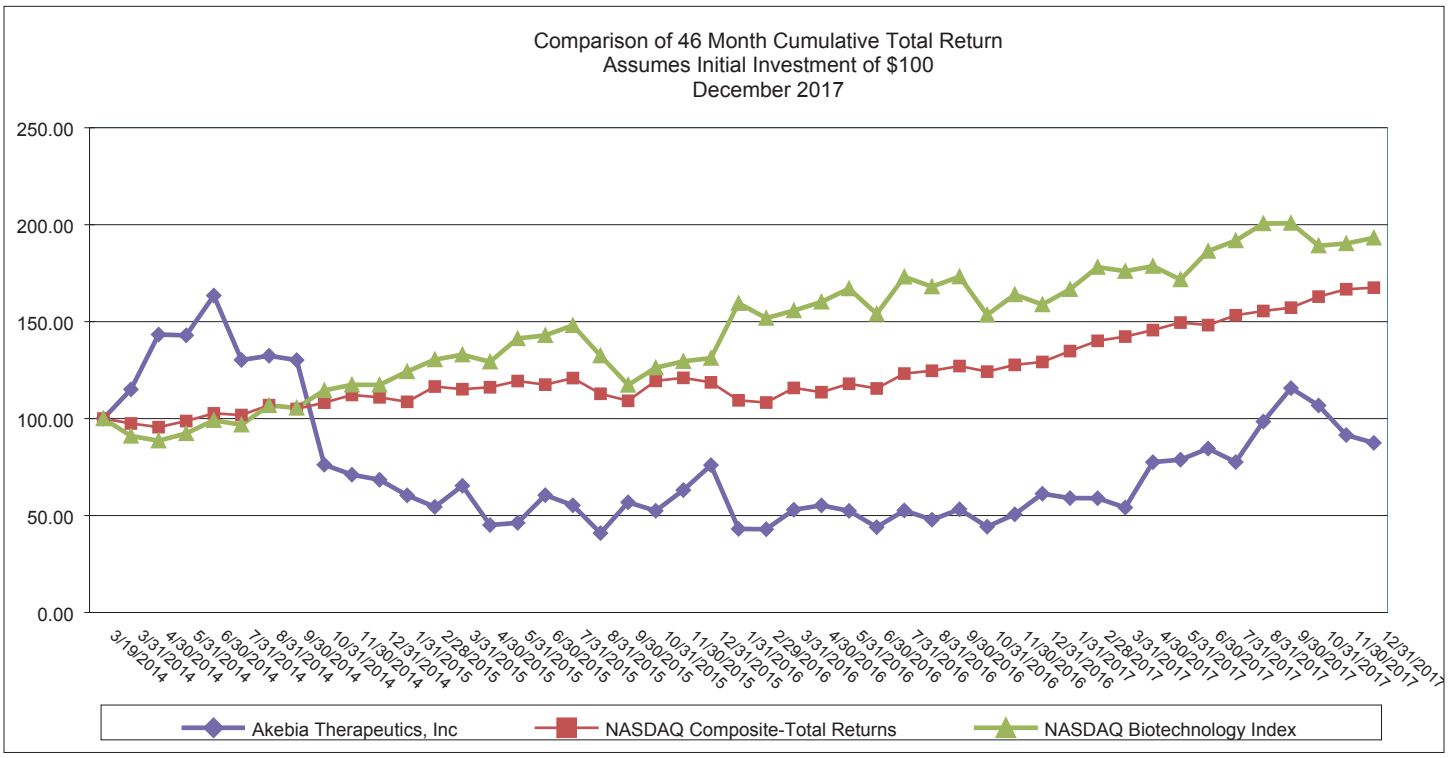
Issuer Purchases of Equity Securities

None.

Comparative Stock Performance Graph

The following performance graph and related information shall not be deemed to be "soliciting material" or "filed" with the SEC or subject to Regulation 14A or 14C, or to the liabilities of Section 18 of the Exchange Act, except to the extent that we specifically request that this information be treated as soliciting material or we specifically incorporate it by reference into a filing under the Securities Act of 1933, 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. The performance shown represents past performance and should not be considered an indication of future performance.



Equity Compensation Plan Information

The following table sets forth information as of December 31, 2017 regarding shares of common stock that may be issued under our equity compensation plans, consisting of our 2008 Equity Incentive Plan, our 2014 Incentive Plan, our 2014 Employee Stock Purchase Plan, and our 2016 Inducement Award Program. As of the closing of our initial public offering, no additional equity awards were made under our 2008 Equity Incentive Plan. Our 2008 Equity Incentive Plan, our 2014 Incentive Plan, and our 2014 Employee Stock Purchase Plan were approved by our shareholders. The 2016 Inducement Award Program was approved by our Board of Directors in May 2016 exclusively for the grant of equity awards to individuals who were not previously an employee or non-employee director of the Company, or following a bona fide period of non-employment, as an inducement material to such individual's entering into employment with the Company, pursuant to Rule 5635(c)(4) of the NASDAQ Listing Rules.

Plan Category	Number of securities to be issued upon exercise of outstanding options, warrants and rights	Weighted-average exercise price of outstanding options, warrants and rights	Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a))
	(a)	(b)	(c)
Equity compensation plans approved by security holders	2,896,514 (1)	$ 8.80 (2)	2,442,890 (3)
Equity compensation plans not approved by security holders (4)	763,500	$ 12.05	750,000 (5)
Total	3,660,014	$ 9.47	3,192,890

(1) Includes 2,896,514 shares of common stock issuable upon the exercise of outstanding options.
(2) Does not include purchase rights accruing under the 2014 Employee Stock Purchase Plan because the purchase right, and therefore the number of shares to be purchased, will not be determined until the end of the purchase period.
(3) As of December 31, 2017, there were 1,790,600 shares of common stock available for grant under the 2014 Incentive Plan and 652,290 shares of common stock available for grant under the 2014 Employee Stock Purchase Plan.
(4) This amount is under the 2016 Inducement Award Program.
(5) Shares approved by our Board of Directors under our 2016 Inducement Award Program for issuance in 2018.

Item 6. Selected Financial Data

The selected consolidated financial data set forth below for the years ended December 31, 2017, 2016 and 2015 and as of December 31, 2017 and 2016 are derived from our audited consolidated financial statements, which are included elsewhere in this Annual Report on Form 10-K. The selected consolidated financial data for the years ended December 31, 2014 and 2013 and as of December 31, 2015, 2014 and 2013 are derived from our audited consolidated financial statements that are not included elsewhere in this Annual Report on Form 10-K. You should read these data together with "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and related notes included elsewhere in this Annual Report on Form 10-K under the captions "Financial Statements and Supplementary Data." The selected financial data in this section are not intended to replace our consolidated financial statements and related notes and are qualified in their entirety by the consolidated financial statements and related notes included elsewhere in this Annual Report on Form 10-K. Our historical results for any prior period are not necessarily indicative of results to be expected in any future period.

	Year Ended December 31,				
	2017	2016	2015	2014	2013
	(in thousands, except share and per share data)				
Consolidated statements of operations data:					
Collaboration revenue	$ 177,984	$ 1,535	$ —	$ —	$ —
Operating expenses:					
Research and development	230,893	115,785	43,016	23,263	8,902
General and administrative	27,008	22,210	18,497	14,677	7,031
Total operating expenses	257,901	137,995	61,513	37,940	15,933
Loss from operations	(79,917)	(136,460)	(61,513)	(37,940)	(15,933)
Other income, net	3,003	713	797	906	2,766
Net loss	$ (76,914)	$ (135,747)	$ (60,716)	$ (37,034)	$ (13,167)
Accretion on preferred stock	—	—	—	(86,899)	(55,886)
Net loss applicable to common shareholders	$ (76,914)	$ (135,747)	$ (60,716)	$ (123,933)	$ (69,053)
Net loss per share applicable to common stockholders—basic and diluted[1]	$ (1.77)	$ (3.60)	$ (2.29)	$ (8.04)	$ (126.94)
Weighted-average number of common shares used in net loss per share applicable to common stockholders—basic and diluted	43,500,795	37,716,949	26,469,170	15,406,386	544,002

(1) See Note 2 of 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.

	2017	2016	December 31, 2015	2014	2013
			(in thousands)		
Consolidated Balance Sheet Data:					
Cash and cash equivalents and available for sale securities	$ 317,792	$ 260,343	$ 138,454	$ 108,918	$ 32,556
Working capital	214,007	182,053	129,149	103,595	29,529
Total assets	364,247	300,216	142,940	110,995	34,665
Redeemable convertible preferred stock	—	—	—	—	157,827
Accumulated deficit	(374,050)	(297,136)	(161,389)	(100,673)	(127,072)
Total stockholders' equity (deficit)	119,331	68,120	130,998	104,078	(127,072)

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 elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve significant 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. Please also refer to the section under the heading "Note Regarding Forward-Looking Statements."

Operating Overview

We are a biopharmaceutical company focused on developing and commercializing 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 and has the potential to set a new standard of care in the treatment of anemia due to chronic kidney disease, or 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 potentially address serious diseases.

HIF, a pathway involving hundreds of genes, is the same pathway used by the body to adapt to lower oxygen availability, or hypoxia, such as that experienced with a moderate increase in altitude. At higher altitudes, the body responds to lower oxygen levels by increasing the availability of HIF, which coordinates the interdependent processes of iron utilization and erythropoietin, or EPO production to increase RBC production and, ultimately, improve oxygen delivery. 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-PHs are inhibited, allowing HIF to stimulate erythropoiesis. These findings have opened up new possibilities for developing therapeutics, such as HIF-PH inhibitors, which have the potential to treat many diseases.

Our lead product candidate, vadadustat, is a HIF-PH inhibitor, or HIF-PHI, in Phase 3 development for the treatment of anemia due to CKD. Anemia is common in patients with CKD, and its prevalence increases as CKD progresses. Anemia is a condition characterized by abnormally low levels of hemoglobin. Hemoglobin is contained within RBCs and carries oxygen to other parts of the body. If there are too few RBCs or if hemoglobin levels are low, the cells in the body will not get enough oxygen. In patients with CKD, anemia results from inadequate EPO levels, which negatively affect RBC production. In addition, iron, which is essential to RBC production, may be deficient in patients with CKD. Left untreated, anemia significantly accelerates overall deterioration of patient health with increased morbidity and mortality. Based on third party prevalence data and company estimates, approximately 37 million people in the United States have CKD and approximately 5.7 million of these individuals suffer from anemia. Anemia from CKD is currently treated by injectable recombinant human erythropoiesis-stimulating agents, or injectable ESAs, such as EPOGEN® (epoetin alfa) and Aranesp® (darbepoetin alfa), or as with iron supplementation or RBC transfusion. Based on publicly available information on sales and market data compiled by a third-party vendor, global sales of injectable ESAs for all uses were estimated to be approximately $7.0 billion in 2016. The vast majority of these sales were for the treatment of anemia due to CKD.

When administered to a patient, injectable ESAs provide supra-physiological levels of exogenous erythropoietin to stimulate production of RBCs. While injectable ESAs can be effective in raising hemoglobin levels, they have the potential to cause significant side effects, and need to be injected subcutaneously or intravenously. In particular, injectable ESAs 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 ESAs. Today, anemia is either not treated or inadequately treated in the majority of non-dialysis dependent, or NDD, CKD patients. There is an unmet need for treatment options that offer an improved safety profile and such agents would have significant market potential.

Vadadustat is designed to stimulate erythropoiesis and effectively treat renal anemia while avoiding the supra-physiologic EPO levels previously observed with injectable ESAs. In addition, vadadustat, if approved, would provide patients with an oral treatment option, rather than an injection. For these reasons, we believe that vadadustat has the potential to set a new standard of care for the treatment of anemia due to CKD.

Phase 1 and Phase 2 data led us to the design of our Phase 3 clinical program for vadadustat. The vadadustat Phase 3 program in NDD-CKD patients with anemia, called PRO_2TECT, and in dialysis dependent, or DD, CKD patients with anemia, called $INNO_2VATE$, is designed to enroll up to approximately 6,900 patients evaluating once daily oral dosing of vadadustat against an injectable ESA active comparator, darbepoetin alfa. The enrollment numbers and the completion of PRO_2TECT and $INNO_2VATE$ will be driven by the accrual 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. As of December 31, 2017, we expect the remaining external aggregate contract research organization, or CRO, costs of PRO_2TECT and $INNO_2VATE$ to be in the range of $420.0 million to $450.0 million. We anticipate reporting top-line clinical data for the PRO_2TECT and $INNO_2VATE$ studies in 2019, subject to the accrual of MACE events. Subject to marketing approvals, we plan to launch vadadustat for the treatment of anemia due to CKD in 2020.

In May 2017, we initiated a Phase 2 study of vadadustat in patients with anemia due to CKD who are on dialysis and do not adequately respond to injectable ESA, or hyporesponders, called FO_2RWARD. Hyporesponders represent approximately 10-15% of subjects with anemia due to DD-CKD, yet they account for 30-40% of total injectable ESA use. These patients have demonstrated a persistently higher risk of mortality than non-hyporesponders, and represent a high unmet need. We believe that, given its differentiated mechanism of action, vadadustat may provide a treatment option for these patients. We are changing the study design to include a broader dialysis population in addition to hyporesponders, and a larger sample size. This study will replace the former FO_2RWARD study. The revised FO_2RWARD study includes once-daily and three-times weekly dosing and is designed to generate data to inform ESA-switching protocols. We expect that we will initiate this study in Q2 2018, with top-line results expected in late 2018 or early 2019.

We had planned to initiate a Phase 3 dosing study, called $TRILO_2GY$, early in 2018 to evaluate three-times weekly dosing of vadadustat patients receiving hemodialysis. Instead, we are replacing this study with a new study design that includes once-daily and three-times weekly dosing and an ESA control, as well as a larger sample size. This study will be designed to generate data to inform switching from Epogen® (epoetin alfa), Aranesp® (darbepoetin alfa) and Mircera® (methoxy PEG-epoetin beta). We expect to initiate this study in late 2018 or early 2019, with top-line results expected in early 2020.

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 the United States. We also granted Otsuka exclusive rights to commercialize vadadustat in Europe, China and certain other markets, subject to marketing approvals. In Japan and certain other countries in Asia, we granted Mitsubishi Tanabe Pharma Corporation, or MTPC, exclusive rights to commercialize vadadustat, subject to marketing approvals. In May 2017, we entered into an exclusive license agreement with Vifor (International) Ltd., or Vifor Pharma, to sell vadadustat solely to Fresenius Kidney Care Group LLC, or FKC, dialysis clinics in the United States subject to approval by the FDA and inclusion of vadadustat in a bundled reimbursement model. During the term of the license agreement, Vifor Pharma may not sell to FKC or its affiliates any HIF product that competes with vadadustat in the United States.

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 as well as in-licensed product candidates, such as AKB-5169. In February 2017, we signed an exclusive agreement with Janssen Pharmaceutica NV, or Janssen, a subsidiary of Johnson & Johnson, 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, or IBD. We intend to complete further preclinical development of this compound, and we are targeting submitting an Investigational New Drug application, or IND, to 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 $76.9 million, $135.7 million and $60.7 million for the years ended December 31, 2017, 2016 and 2015, 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:

- conduct our development program of vadadustat for the treatment of anemia due to CKD, including PRO_2TECT, $INNO_2VATE$, FO_2RWARD and $TRILO_2GY$, and develop plans for the preclinical and clinical development of any other potential product candidates;
- seek marketing approvals for our product candidates that successfully complete clinical studies and maintain such marketing approvals, including complying with any post-marketing regulatory requirements;
- 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 vadadustat and any other product candidates;
- seek to discover and develop additional product candidates;
- engage in transactions, including strategic transactions, merger, collaboration, acquisition and licensing arrangements, pursuant to which we would market and develop commercial products, or develop other product candidates and technologies;
- make royalty, milestone or other payments under our license agreement with Janssen and any future in-license agreements;
- maintain, protect and expand our intellectual property portfolio;
- attract and retain skilled personnel;
- continue to create additional infrastructure and expend additional resources to support our operations as a public company, including any additional infrastructure and resources necessary to support a transition from our status as an emerging growth company; and
- experience any delays or encounter issues with any of the above.

We do not expect to generate revenue from product sales unless and until we successfully complete development and obtain marketing 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 CROs to carry out our clinical development activities, and we do not yet have a sales organization. If we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. If and until we can generate a sufficient amount of revenue from product sales, we expect to finance future cash needs through public or private equity or debt offerings, payments from our collaborators, strategic transactions, or a combination of these approaches. If we are unable to raise additional capital in sufficient amounts when needed 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. Any of these events could significantly harm our business, financial condition and prospects.

Through 2017, we raised approximately $373.1 million of net proceeds from the sale of equity including $292.6 million from various underwritten public offerings, $30.5 million from an at-the-market offering, or ATM, pursuant to sales agreements with Cantor Fitzgerald & Co and $50.0 million from the sale of 3,571,429 shares of common stock to Vifor Pharma. At inception of our collaboration agreements with Otsuka and MTPC, they committed to approximately $573.0 million or more in cost-share funding, of which we generally continue to receive on a quarterly prepaid basis, and license payments. Of these commitments, we received approximately $272.0 million at the onset of the collaboration agreements.

Financial Overview

In the quarter ended June 30, 2017, we identified and corrected an immaterial error in the amount of research and development expenses related to our global Phase 3 clinical program of vadadustat. This adjustment also affected the amount of revenue recognized pursuant to our license and collaboration agreements with Otsuka. The adjustments impacted our results of operations in each quarter of 2016 and the first quarter of 2017. We concluded the effect of these adjustments was not material to our consolidated financial statements for any prior period.

Revenue

To date, we have not generated any revenue from the sales of products. Our revenues have been derived from collaboration revenues, which include license and milestone revenues and cost-sharing revenue, generated through collaboration and license agreements with partners for the development and commercialization of vadadustat. Cost-sharing revenue represents amounts reimbursed by our collaboration partners for expenses incurred by us for research and development activities and, potentially, co-promotion activities, under our collaboration agreements.

The Company recognizes revenue in accordance with 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.

With regards to the MTPC and Otsuka collaboration agreements, the Company recognizes revenue related to amounts allocated to the License Unit of Accounting on a proportional performance basis as the underlying services are performed. 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. For additional information on our revenue recognition policy related to multiple-element arrangements, see the section titled "Summary of Significant Accounting Policies – Revenue Recognition."

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 into which we may enter.

Research and Development Expenses

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

personnel-related expenses, including salaries, benefits, recruiting fees, travel and stock-based compensation expense of our research and development personnel;

expenses incurred under agreements with CROs and investigative sites that conduct our clinical studies;

the cost of acquiring, developing and manufacturing clinical study materials through CMOs;

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, clinical and regulatory 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 marketing approval. We may never succeed in achieving marketing 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 and other preclinical and clinical studies of vadadustat and any other product candidates;

difficulties or delays in enrolling patients in our clinical trials;

assuming favorable Phase 3 clinical results, the cost, timing and outcome of obtaining marketing approvals for vadadustat and any other product candidates in the United States, Europe and other jurisdictions;

the cost of having our product candidates manufactured and obtaining comparator product 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;

addition and retention of key research and development personnel;

unanticipated changes to laws or regulations applicable to our clinical trials; and

continued acceptable safety profiles of any approved products following approval.

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 other regulatory authorities were to require us to conduct clinical studies in addition to or different from those that we currently anticipate, or if we experience 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, 2017, we have incurred $462.8 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 any other product candidates. Our current and/or planned research and development activities include the following:

global development of vadadustat;

research and development of compounds in our HIF portfolio, including our product candidate, AKB-5169; and

diversification of 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 drug substance and drug product manufacturing for clinical studies.

We currently have four programs to which our research and development costs are attributable. We have not accumulated and tracked our research and development costs or our personnel and personnel-related costs on a program-by-program basis as our employee and infrastructure resources, and many of our costs, are directed broadly to applicable research endeavors. As a result, we are unable to specify precisely the 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), and 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 measurable 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 the proportional performance method, 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 manufacturing, development and distribution of clinical material.

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, shares of common stock and warrants. We account for our stock-based compensation awards in accordance with 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 a blend of our stock price and 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 limited company-specific historical and implied volatility data for trading our stock in the public market, we have based our estimate of expected volatility in part 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. During 2017, we began to estimate our volatility by using a blend of our stock price history for the length of time we have market data for our stock and the historical volatility of similar public companies for the expected term of each grant. We are a company in the product development stage with no product 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.

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.

The Company adopted ASU No. 2016-09, *Compensation-Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting,* effective in the first quarter of the year ended December 31, 2017. Prior to adoption, share-based compensation expense was recognized on a straight line basis, net of estimated forfeitures, such that expense was recognized only for share-based awards that are expected to vest. A forfeiture rate was estimated annually and revised, if necessary, in subsequent periods if actual forfeitures differed from initial estimates. Effective upon adoption, we no longer apply a forfeiture rate and instead account for forfeitures as they occur.

Stock-based compensation expense totaled approximately $12.3 million, $5.8 million and $4.7 million for the years ended December 31, 2017, 2016 and 2015, respectively.

We expect the impact of our stock-based compensation expense for stock options and RSUs granted to employees and non-employees to grow in future periods due to potential increases in the fair value of our common stock and an anticipated increase in the number of grants as a result of a planned 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, 2017 and 2016

	Year ended December 31,		Increase
	2017	2016	(Decrease)
		(In Thousands)	
Collaboration revenue	$ 177,984	$ 1,535	$ 176,449
Operating expenses:			
Research and development	230,893	115,785	115,108
General and administrative	27,008	22,210	4,798
Total operating expenses	257,901	137,995	119,906
Loss from operations	(79,917)	(136,460)	(56,543)
Other income, net	3,003	713	2,290
Net loss	$ (76,914)	$ (135,747)	$ (58,833)

Collaboration Revenue. Collaboration revenue was $178.0 million for the year ended December 31, 2017, compared to $1.5 million for the year ended December 31, 2016. We recognized $1.5 million in collaboration revenue for the year ended December 31, 2016 from our cost sharing arrangement under the Otsuka U.S. Agreement which commenced in December 2016, and no collaboration revenue from MTPC as the revenue recognition criteria for the MTPC Agreement, as required under ASC 605, had not yet been satisfied. The increase in revenue between the two periods was attributable to an additional $136.7 million of revenue recognized under both the Otsuka U.S. Agreement and Otsuka International Agreement which was consummated in April 2017, as well as $39.7 million of revenue recognized in connection with the MTPC agreement as the revenue recognition criteria as required under ASC 605 was satisfied in the fourth quarter of 2017.

Research and Development Expenses. Research and development expenses were $230.9 million for the year ended December 31, 2017, compared to $115.8 million for the year ended December 31, 2016. The increase of $115.1 million was due to the following:

	(in millions)
PRO_2TECT and $INNO_2VATE$ Phase 3 program	$ 85.8
FO_2RWARD and $TRILO_2GY$ studies	6.3
Japan Phase 2 studies	5.7
Regulatory activities and other clinical and preclinical activities	3.0
Manufacture of drug substance	0.5
Total increase related to the continued development of vadadustat	101.3
Headcount, consulting and facilities	8.2
Fair value of warrants issued for Janssen license	3.4
Janssen license fee	1.1
Other	1.1
Total net increase	$ 115.1

The increase in the costs related to the development of vadadustat is primarily attributable to an increase in external costs related to the continued advancement of the PRO_2TECT and $INNO_2VATE$ Phase 3 program, including ongoing enrollment, the Phase 2 studies in Japan, and study commencement activities for the FO_2RWARD and $TRILO_2GY$ studies, both of which have been replaced with new study designs. We expect to incur a total of approximately $21.4 million for the Phase 2 studies in Japan of which MTPC has already paid $20.0 million and MTPC will reimburse us for the remaining costs once incurred. The increase in headcount, consulting and facility related costs relates to additional resources required to support our expanding research and development programs. We expect our research and development expenses to significantly increase in future periods in support of our global Phase 3 program and other studies for vadadustat, development of AKB-5169 and any future product candidates.

General and Administrative Expenses. General and administrative expenses were $27.0 million for the year ended December 31, 2017, compared to $22.2 million for the year ended December 31, 2016. The increase of $4.8 million was primarily due to an increase in costs to support our research and development programs, including headcount and compensation-related costs and associated facility-related costs. We expect our general and administrative expenses to increase in future periods to support our continued research and development and potential commercialization of vadadustat and other product candidates.

Other Income, Net. Other income, net, was $3.0 million for the year ended December 31, 2017, compared to $0.7 million for the year ended December 31, 2016. Other income, net for the year ended December 31, 2017, was primarily comprised of interest income caused by higher average investment balances during 2017. Other income, net for the year ended December 31, 2016 consisted of interest income of $0.9 million offset by expenses related to the write-off of capitalized software.

Comparison of the Years Ended December 31, 2016 and 2015

	Year ended December 31,		Increase
	2016	2015	(Decrease)
		(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 Otsuka U.S. Agreement.

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)
PRO_2TECT and $INNO_2VATE$ Phase 3 program	$ 65.5
Manufacture of drug substance	3.1
Regulatory and other clinical and preclinical 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_2TECT and $INNO_2VATE$ Phase 3 studies. The increase in headcount, consulting and facility related costs is primarily due to additional headcount and consulting costs to support the global Phase 3 program 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 global Phase 3 program 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.

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, 2017, we had an accumulated deficit of $374.1 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 sales of our common stock and payments received from our collaboration partners. As of December 31, 2017, we had cash and cash equivalents and available for sale securities of approximately $317.8 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,		
	2017	2016	2015
		(In Thousands)	
Net cash provided by (used in):			
Operating activities	$ (56,159)	$ 57,906	$ (52,407)
Investing activities	(177,260)	12,705	(13,688)
Financing activities	116,240	66,946	83,093
Net increase/(decrease) in cash and cash equivalents	$ (117,179)	$ 137,557	$ 16,998

Operating Activities. The cash provided or used for operating activities in all periods resulted primarily from our net losses adjusted for non-cash charges and changes in the components of working capital. The net cash used by operating activities during the year ended December 31, 2017 of $56.2 million was largely driven by our Phase 3 development program for vadadustat, partially offset by receipt of cash from collaboration agreements, including a $73.0 million up-front payment under the Otsuka International Agreement. The net cash provided by operating activities during the year ended December 31, 2016 of $57.9 million was primarily the result of cash received from collaboration agreements, including $158.8 million received at inception from the Otsuka U.S. Agreement, partially offset by our Phase 3 development program for vadadustat. The net cash used by operating activities during the year ended December 31, 2016 of $52.4 million was largely driven by our Phase 2 and Phase 3 development program.

Investing Activities. During the years ended December 31, 2017 and 2015, our investing activities used net cash of $177.3 million and $13.7 million, respectively. During the year ended December 31, 2016, our investing activities provided net cash of $12.7 million. The net cash used by investing activities in 2017 was comprised primarily from the purchases of available for sale securities of $330.6 million, partially offset by sale of and maturities of available for sale securities and purchases of equipment. Net cash provided by investing activities in 2016 was comprised primarily from the maturities of available for sale securities, partially offset by purchases in available for sale securities and purchases of equipment. Net cash used in investing activities for the year ended December 31, 2015 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, 2017, 2016 and 2015 our net cash provided by financing activities was $116.2 million, $66.9 million and $83.1 million, respectively. Net cash provided by financing activities for the years ended December 31, 2017, 2016 and 2015 consisted primarily of net proceeds from the issuance of common stock from our follow-on public offerings and ATM offerings.

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 marketing 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 marketing 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 continue 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 2017 with cash, cash equivalents and available for sale securities of $317.8 million. At inception of our collaboration agreements with Otsuka and MTPC, they committed to approximately $573.0 million or more in cost-share funding, of which we generally continue to receive on a quarterly prepaid basis, and license payments. Of these commitments, we received approximately $272.0 million at the onset of the collaboration agreements. We expect our existing cash resources, including the timing of committed research and development funding from its collaborators, to fund our current operating plan into the second quarter of 2019.

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 or debt offerings, payments from our collaborators, strategic transactions, or a combination of these approaches. 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. Furthermore, our development milestones may not be achieved, we may not receive the anticipated funding from our collaboration partners, and we may not secure other sources of financing. 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 I, 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 May 2017, collectively, the Lease. Total monthly lease payments under the initial base rent are approximately $242,000 and is subject to annual rent escalations. In addition to such annual rent escalations, base rent payments for a portion of the said premises commenced on 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 $70,526 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 with respect to the lab space expires on November 30, 2021, 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 in the form of a letter of credit is included in other assets in our consolidated balance sheets as of December 31, 2017 and December 31, 2016.

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 consolidated balance sheets as of December 31, 2017 and December 31, 2016.

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, or 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 $0.3 million. The total security deposit in connection with the Sublease of $21,432 is included in other current assets and other liabilities in the Company's consolidated balance sheets.

At December 31, 2017, 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
Operating Lease Obligations	$ 30,444	$ 3,579	$ 7,301	$ 6,991	$ 12,573
Less: Sublease Income	(257)	(257)	—	—	—
Total	$ 30,187	$ 3,322	$ 7,301	$ 6,991	$ 12,573

(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 $0.3 million of sublease rental income that we are entitled to receive through 2018.

Under our agreement with IQVIA, formerly known as Quintiles IMS, to provide services for the PRO_2TECT and $INNO_2VATE$ programs, the total remaining contract costs as of December 31, 2017 were approximately $276.4 million. The estimated period of performance for the committed work with IQVIA is through the first quarter of 2020. We contract with various other organizations to conduct research and development activities with remaining contract costs to us of approximately $52.4 million as of December 31, 2017. The scope of the services under these research and development contracts can be modified and the contracts cancelled by us upon written notice, and therefore not included in the table of contractual obligations and commitments. In some instances, the contracts may be cancelled by the third party upon written notice.

Off-Balance Sheet Arrangements

As of December 31, 2017, 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, 2017 and 2016, we had cash and cash equivalents and available for sale securities of $317.8 million and $260.3 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.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Akebia Therapeutics, Inc. (the "Company") as of December 31, 2017 and 2016, and the related consolidated statements of operations and comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2017, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the consolidated financial position of the Company at December 31, 2017 and 2016, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2017, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

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

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting 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.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2013.

Boston, Massachusetts
March 12, 2018

AKEBIA THERAPEUTICS, INC.

Consolidated Balance Sheets

(in thousands, except share and per share data)

	December 31, 2017	December 31, 2016
Assets		
Current assets:		
Cash and cash equivalents	$ 70,156	$ 187,335
Available for sale securities	247,636	73,008
Accounts receivable	34,216	33,823
Prepaid expenses and other current assets	6,348	2,155
Total current assets	358,356	296,321
Property and equipment, net	3,617	2,612
Other assets	2,274	1,283
Total assets	$ 364,247	$ 300,216
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 6,998	$ 2,039
Accrued expenses	52,441	30,261
Short-term deferred revenue	84,910	81,968
Total current liabilities	144,349	114,268
Deferred rent, net of current portion	2,588	2,480
Deferred revenue, net of current portion	97,957	115,321
Other non-current liabilities	22	27
Total liabilities	244,916	232,096
Commitments and contingencies (Note 10)		
Stockholders' equity:		
Preferred stock $0.00001 par value, 25,000,000 shares authorized at December 31, 2017 and 2016; 0 shares issued and outstanding at December 31, 2017 and 2016	—	—
Common stock: $0.00001 par value; 175,000,000 shares authorized at December 31, 2017 and 2016; 47,612,619 and 38,615,709 shares issued and outstanding at December 31, 2017 and 2016, respectively	—	—
Additional paid-in capital	493,823	365,298
Accumulated other comprehensive income (loss)	(442)	(42)
Accumulated deficit	(374,050)	(297,136)
Total stockholders' equity	119,331	68,120
Total liabilities and stockholders' equity	$ 364,247	$ 300,216

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,		
	2017	2016	2015
Collaboration revenue	$ 177,984	$ 1,535	$ —
Operating expenses:			
Research and development	230,893	115,785	43,016
General and administrative	27,008	22,210	18,497
Total operating expenses	257,901	137,995	61,513
Operating loss	(79,917)	(136,460)	(61,513)
Other income (expense):			
Interest income	2,799	901	510
Other income/(expense)	204	(188)	287
Net loss	$ (76,914)	$ (135,747)	$ (60,716)
Net loss per share - basic and diluted	$ (1.77)	$ (3.60)	$ (2.29)
Weighted-average number of common shares - basic and diluted	43,500,795	37,716,949	26,469,170
Comprehensive loss:			
Net loss	$ (76,914)	$ (135,747)	$ (60,716)
Other comprehensive loss - unrealized loss on securities	(400)	(42)	(234)
Total comprehensive loss	$ (77,314)	$ (135,789)	$ (60,950)

See accompanying notes to consolidated financial statements.

Akebia Therapeutics, Inc.

Consolidated Statements of Stockholders' Equity

(in thousands, except share and per share data)

	Common Stock		Additional				Total
	Number of Shares	$0.00001 Par Value	Paid-In Capital	Treasury Stock	Unrealized Gain/Loss	Accumulated Deficit	Stockholders' Equity
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 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 issuance costs	7,865,293	—	66,623	—	—	—	66,623
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 loss	—	—	—	—	—	(135,747)	(135,747)
Balance at December 31, 2016	38,615,709	$ —	$ 365,298	$ —	$ (42)	$ (297,136)	$ 68,120
Issuance of common stock, net of issuance costs	8,672,270	—	114,580	—	—	—	114,580
Proceeds from sale of stock under employee stock purchase plan	44,833	—	353	—	—	—	353
Forfeitures of restricted common stock	(2,406)	—	—	—	—	—	—
Exercise of options	256,213	—	1,312	—	—	—	1,312
Share-based compensation expense	—	—	8,867	—	—	—	8,867
Restricted stock unit vesting	26,000	—	—	—	—	—	—
Issuance of common stock warrants	—	—	3,413	—	—	—	3,413
Unrealized gain/loss	—	—	—	—	(400)	—	(400)
Net loss	—	—	—	—	—	(76,914)	(76,914)
Balance at December 31, 2017	47,612,619	$ —	$ 493,823	$ —	$ (442)	$ (374,050)	$ 119,331

See accompanying notes to consolidated financial statements.

AKEBIA THERAPEUTICS, INC.

Consolidated Statements of Cash Flows

(in thousands)

	Year ended December 31,		
	2017	2016	2015
Operating activities:			
Net loss	$ (76,914)	$ (135,747)	$ (60,716)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	617	296	96
Amortization of premium/discount on investments	610	494	558
Loss on disposal of property and equipment	—	306	—
Stock-based compensation	8,867	5,825	4,714
Fair value of warrants issued for license	3,413	—	—
Changes in operating assets and liabilities:			
Accounts receivable	(393)	(33,823)	—
Prepaid expenses and other current assets	(4,193)	428	(1,001)
Other long-term assets	(991)	(2)	(976)
Accounts payable	4,959	(274)	231
Accrued expense	21,974	20,703	4,646
Deferred revenue	(14,422)	197,289	—
Deferred rent	314	2,411	41
Net cash provided by (used in) operating activities	(56,159)	57,906	(52,407)
Investing activities:			
Purchase of equipment	(1,622)	(2,662)	(414)
Proceeds from the maturities of available for sale securities	149,998	162,376	63,901
Proceeds from sales of available for sale securities	5,000	—	—
Purchase of available for sale securities	(330,636)	(147,009)	(77,175)
Net cash provided by (used in) investing activities	(177,260)	12,705	(13,688)
Financing activities:			
Proceeds from the issuance of common stock, net of issuance costs	114,580	66,736	82,750
Proceeds from the sale of stock under employee stock purchase plan	353	106	220
Proceeds from the exercise of stock options	1,312	124	130
Payments on capital lease obligations	(5)	(20)	(7)
Net cash provided by financing activities	116,240	66,946	83,093
Increase in cash and cash equivalents	(117,179)	137,557	16,998
Cash and cash equivalents at beginning of the period	187,335	49,778	32,780
Cash and cash equivalents at end of the period	$ 70,156	$ 187,335	$ 49,778
Non-cash financing activities			
Unpaid follow-on offering costs	$ —	$ 12	$ 102
Assets acquired under capital lease	$ —	$ —	$ 12

See accompanying notes to consolidated financial statements.

1. Nature of Organization and Operations

Akebia Therapeutics, Inc., referred to as Akebia or the Company, was incorporated in the State of Delaware in 2007. Akebia is a biopharmaceutical company focused on developing and commercializing novel therapeutics for patients based on hypoxia-inducible factor, or HIF, biology, and building its pipeline while leveraging its 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. The Company's lead product candidate, vadadustat, is an oral therapy in Phase 3 development, and has the potential to set a new standard of care in the treatment of anemia due to chronic kidney disease, or 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 potentially address serious diseases.

Since inception, the Company has devoted most of its resources to research and development, including its preclinical and clinical development activities, raising capital, and providing general and administrative support for these operations. 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 marketing 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 global Phase 3 program for vadadustat in non-dialysis dependent, or NDD-CKD, called PRO_2TECT, and dialysis dependent, or DD-CKD, called $INNO_2VATE$, risks of clinical trial failures, the risk of relying on third parties, the risk that the Company never achieves profitability, protection of proprietary technology, compliance with governmental regulations, and dependence on key personnel. In December 2015 the first subject was dosed in PRO_2TECT, and the first subject was dosed in $INNO_2VATE$ in August 2016. Overall, the PRO_2TECT and $INNO_2VATE$ Phase 3 programs are designed to enroll up to approximately 6,900 patients. The enrollment numbers and the completion of PRO_2TECT and $INNO_2VATE$ will be subject to the accrual of major adverse cardiovascular events, or MACE. The Company anticipates reporting top-line clinical data for the PRO_2TECT and $INNO_2VATE$ studies in 2019, subject to the accrual of MACE events. Subject to marketing approvals, we plan to launch vadadustat for the treatment of anemia due to CKD in 2020.

Through 2017 the Company raised approximately $373.1 million of net proceeds, including $292.6 million from several underwritten public offerings, $30.5 million from an at-the-market offering, or ATM, pursuant to sales agreements with Cantor Fitzgerald & Co. and $50.0 million from the sale of 3,571,429 shares of common stock to Vifor (International) Ltd., or Vifor Pharma. At inception of our collaboration agreements with Otsuka Pharmaceutical Co. Ltd., or Otsuka and Mitsubishi Tanabe Pharma Corporation, or MTPC, they committed to approximately $573.0 million or more in cost-share funding, of which we generally continue to receive on a quarterly prepaid basis, and license payments. Of these commitments, we received approximately $272.0 million at the onset of the collaboration agreements.

In December 2015, the Company entered into a collaboration agreement with MTPC to develop and commercialize vadadustat in Japan and certain other countries in Asia, collectively, the MTPC Territory, for total payments of up to $245.0 million, comprised of a $20.0 million upfront payment, up to $50.0 million in specified development and regulatory milestones, and up to $175.0 million in specified commercial milestones, as well as tiered double-digit royalty payments up to 20% on sales of vadadustat in the MTPC Territory (Note 3).

In December 2016, the Company entered into a collaboration and license agreement with Otsuka to develop and commercialize vadadustat in the United States. In December 2016, the Company received $125.0 million upfront payment, and in March 2017, Otsuka reimbursed the Company 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 $153.6 million or more, depending on the actual global development costs incurred. In addition, Akebia is eligible to receive from Otsuka up to $190.0 million in specified development and regulatory milestones and up to $575.0 million in specified 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 (Note 3).

In April 2017, the Company entered into a collaboration and license agreement with Otsuka to develop and commercialize vadadustat in Europe, Russia, China, Canada, Australia, the Middle East and certain other territories. In April 2017, the Company received a $73.0 million upfront payment and $0.2 million for global expenses previously incurred by the Company in implementing the current global development plan for vadadustat in DD-CKD and NDD-CKD patients in excess of a specified threshold during the quarter-ended March 31, 2017. The agreement also provides for additional funding for the global development program for vadadustat, totaling $163.6 million or more, depending on the actual global development costs incurred. In addition, Akebia is eligible to receive from Otsuka up to $132.0 million in specified development and regulatory milestones and up to $525.0 million in specified commercial milestones (Note 3).

The Company believes that its existing cash and cash equivalents and available for sale securities of approximately $317.8 million at December 31, 2017, together with the committed funding from its collaboration partners, will be sufficient to allow the Company to fund its current operating plan into the second quarter of 2019, and as a result, through at least twelve months from the filing of the Company's 2017 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. The Company will require additional capital for the further development of our existing product candidates and will need to raise additional funds to pursue development activities related to additional product candidates. If and until the Company can generate a sufficient amount of revenue from our products, we expect to finance future cash needs through public or private equity or debt offerings, payments from our collaborators, strategic transactions, or a combination of these approaches.

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 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 June 30, 2017, the Company identified and corrected an immaterial error in the amount of research and development expenses related to the Company's global Phase 3 program of vadadustat. This adjustment also affected the amount of revenue recognized pursuant to the Company's license and collaboration agreements with Otsuka. The adjustments impacted our results of operations in each quarter of 2016 and the first quarter of 2017. The Company concluded the effect of these adjustments was not material to its consolidated financial statements for any prior period.

New Accounting Pronouncements – Recently Adopted

The Company adopted ASU No. 2016-09, *Compensation-Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting,* effective in the first quarter of the year ended December 31, 2017. This ASU simplifies 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. The following summarizes the effects of the adoption on the Company's audited consolidated financial statements:

Income taxes - Upon adoption of this standard, all excess tax benefits and tax deficiencies, including tax benefits of dividends on share-based payment awards, are recognized as income tax expense or benefit in the income statement. The tax effects of exercised or vested awards are treated as discrete items in the reporting period in which they occur. The Company also recognizes excess tax benefits regardless of whether the benefit reduces taxes payable in the current period. The Company has applied the modified retrospective adoption approach beginning in fiscal year 2017 and prior periods have not been adjusted. As a result, the Company will establish a net operating loss deferred tax asset of $0.4 million to account for prior period excess tax benefits through retained earnings, however an offsetting valuation allowance of $0.4 million will also be established through retained earnings because it is not more likely than not that the deferred tax asset will be realized due to historical and expected future losses, such that there is no impact on the Company's consolidated financial statements.

Forfeitures - Prior to adoption, share-based compensation expense was recognized on a straight-line basis, net of estimated forfeitures, such that expense was recognized only for share-based awards that are expected to vest. A forfeiture rate was estimated annually and revised, if necessary, in subsequent periods if actual forfeitures differed from initial estimates. Upon adoption of this standard, the Company will no longer apply a forfeiture rate and instead will account for forfeitures as they occur. As the Company previously estimated forfeitures to determine stock-based compensation expense, this change in accounting principle resulted in a cumulative-effect adjustment as of January 1, 2017 to reduce retained earnings by $0.2 million.

Earnings Per Share - The Company uses the treasury stock method to compute diluted earnings per share, unless the effect would be anti-dilutive. Under this method, the Company will no longer be required to estimate the tax rate and apply it to the dilutive share calculation for determining the dilutive earnings per share. The Company has applied this methodology beginning in fiscal year 2017, and prior periods have not been adjusted.

Upon adoption in January 2017, no other aspects of ASU 2016-09 had a material effect on the Company's unaudited condensed consolidated financial statements or related footnote disclosures.

In January 2017, the FASB issued an ASU 2017-01, *Business Combinations (Topic 805) Clarifying the Definition of a Business*. ASU 2017-01 clarifies the definition of a business with the objective of adding guidance to assist entities with evaluating whether transactions should be accounted for as acquisitions (or disposals) of assets or businesses. The definition of a business affects many areas of accounting including acquisitions, disposals, goodwill, and consolidation. The guidance is effective for annual periods beginning after December 15, 2017, including interim periods within those periods. ASU 2017-01 may be adopted early. The Company adopted the provisions of ASC 2017-01 effective January 1, 2017. Adoption did not have a material impact on the Company's financial position, results of operations, or cash flows.

New Accounting Pronouncements – Not Yet Adopted

In May 2014, the FASB issued ASU 2014-09, *Revenue from Contracts with Customers (Topic 606)*, 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 was 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 for all periods presented in the period of adoption (with some limited relief provided) or a modified retrospective method.

The Company’s historical revenue has been derived from its collaboration agreements with Otsuka Pharmaceutical Co. Ltd., or Otsuka. The Company commenced revenue recognition under its collaboration agreement with Mitsubishi Tanabe Pharma Corporation, or MTPC, upon initiation of delivery of the clinical supply of vadadustat to MTPC for the Phase 3 studies of vadadustat sponsored by MTPC in Japan, which occurred in the fourth quarter of 2017. These arrangements contain multiple-elements and have been accounted for pursuant to ASC Topic 605-25, Revenue Recognition Multiple-Element Arrangements, or ASC 605-25.

The new revenue standard creates ASC Topic 606, *Revenue from Contracts with Customers*, or ASC 606. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize when (or as) the entity satisfies a performance obligation. ASC 606 also impacts certain other areas, such as the accounting for costs to obtain or fulfill a contract. The standard also requires disclosure of the nature, amount, timing, and uncertainty of revenue and cash flows arising from contracts with customers.

The Company will adopt the new standard effective January 1, 2018, using the full retrospective transition method. Under this method, the Company will revise its results for the years ended December 31, 2016 and 2017, as well as the applicable interim periods within those years as if ASC 606 had been effective for those periods. The Company has assessed the effect of adoption of this standard as it relates to its collaboration agreements with Otsuka and MTPC. Currently, the Company anticipates the effects of adoption to be as described below. Estimated impacts from the adoption of this standard could differ upon the final adoption and implementation of the standard.

The Company expects the accounting for contingent milestone payments to be the most significant change in the accounting for its collaboration agreements. Under ASC 605-28, *Revenue Recognition-Milestone Method*, the Company evaluates at inception of an arrangement whether each milestone is substantive and at risk to both parties on the basis of the contingent nature of the milestone. Milestones that are considered substantive are recognized as revenue in their entirety upon achievement, assuming all other revenue 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. However, under ASC 606, there is no specific guidance as it relates to milestone payments. Therefore, under the new standard, milestone payments are to be considered in accordance with the overall model of ASC 606, which requires an assessment at each reporting date of the probability of achievement of the milestone and the likelihood that a significant reversal in the cumulative amount of revenue recognized will not occur. This assessment may result in contingent milestone payments being recognized before the milestone event has occurred and therefore would result in revenue being recognized earlier than under ASC 605. In addition, ASC 606 changes guidance regarding the accounting for variable consideration received from licensees, which may impact the estimation of, and determination of the timing of, the related revenue recognition.

With respect to the collaboration agreements with Otsuka, the Company currently estimates no impact to revenue for the years ended December 31, 2017 and 2016 after the adoption of ASC 606. With respect to the MTPC collaboration agreement, the Company estimates an increase in revenue of $3.2 million and $0 for the years ended December 31, 2017 and 2016, respectively, after the adoption of ASC 606. The change in revenue is due to the timing of when milestone payments can be recognized under the new standard as well as the period over which this revenue is recognized. As noted in the previous paragraph, under ASC 605-28, certain milestones that are considered substantive at inception of an arrangement are recognized as revenue in their entirety upon achievement. However, under ASC 606, these substantive milestone payments would be classified as variable consideration and included in the allocable transaction price over the remaining period of performance when it is probable that a significant reversal in the cumulative amount of revenue recognized would not occur.

In addition to the effects on collaboration revenue, the Company expects to revise balances of working capital components associated with collaboration revenues, such as accounts receivable and deferred revenue. Overall, the Company currently expects current assets to increase as a result of these changes by $3.2 million and $0 as of December 31, 2017 and 2016, respectively, and it currently expects no changes in current liabilities for both December 31, 2017 and 2016.

The quantitative changes provided above are estimates of the expected effects of the Company's adoption of ASC 606. These changes represent management's best estimates of the effects of adopting ASC 606 at the time of the preparation of this Annual Report on Form 10-K. The actual, final quantitative effects of the adoption of ASC 606 are subject to change from these estimates and such change may be significant, pending the completion of the Company's assessment in the first quarter of 2018.

Finally, ASC 606 requires more robust disclosures than required by previous guidance, including disclosures related to disaggregation of revenue into appropriate categories, performance obligations, the judgments made in revenue recognition determinations, adjustments to revenue which relate to activities from previous quarters or years, any significant reversals of revenue, and costs to obtain or fulfill contracts.

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 entities to recognize right-of-use assets and lease liabilities on their balance sheets and provide enhanced disclosures. The amendments in ASU 2016-02 are effective for fiscal years beginning after December 15, 2018 and interim periods within those fiscal years. Early application is permitted for all entities, however, at this time, the Company does not intend to early adopt. 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 and related disclosures.

In October 2016, the FASB issued ASU 2016-18, *Restricted Cash*, which requires that a statement of cash flows explain the change during the period in the total of cash, cash equivalents, and amounts generally describes as restricted cash or restricted cash equivalents. Therefore, amounts generally described as restricted cash and restricted cash equivalents should be included with cash and cash equivalents when reconciling the beginning-of-period and end-of-period total amounts shown on the statement of cash flows. ASU 2016-18 is effective for fiscal years beginning after December 15, 2017, and interim periods within those years, using a retrospective transition method to each period presented. Early adoption is permitted. The Company is evaluating the potential impact that the adoption of ASU 2016-18 will have on the Company's financial position or results of operations.

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 novel therapeutics for patients based on HIF biology and building its pipeline while leveraging its development and commercial expertise in renal disease.

Derivative Financial Instruments

The Company accounts for warrants and other derivative financial instruments as either equity or liabilities in accordance with ASC Topic 815, *Derivatives and Hedging,* or ASC 815, based upon the characteristics and provisions of each instrument. Warrants classified as equity are recorded at fair value as of the date of issuance on the Company's consolidated balance sheets and no further adjustments to their valuation are made. Warrants classified as derivative liabilities and other derivative financial instruments that require separate accounting as liabilities are recorded on the Company's consolidated balance sheets at their fair value on the date of issuance and will be revalued on each subsequent balance sheet date until such instruments are exercised or expire, with any changes in the fair value between reporting periods recorded as other income or expense. The warrant issued by the Company in connection with the Janssen Pharmaceutica NV Research and License Agreement, the Janssen Agreement, is classified as equity in the Company's consolidated balance sheet. (See Note 7).

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, revenue and income taxes.

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. Cash equivalents are reported at fair value. At December 31, 2017, the Company's cash equivalents are 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, 2017. 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.

Accounts Receivable

The Company's accounts receivable represents amounts due to the Company from its collaboration agreements with MTPC and Otsuka (see Note 3). Reimbursable costs that have not been invoiced as of the balance sheet date are recorded as unbilled accounts receivable. The Company makes judgments as to its ability to collect outstanding receivables and provides an allowance for receivables when collection becomes doubtful. Provisions are made based upon a specific review of all significant outstanding invoices and the overall quality and age of those invoices not specifically reviewed. The Company believes that credit risks associated with its collaboration partners are not significant. To date, the Company has not had any write-offs of bad debt, and the Company did not have an allowance for doubtful accounts as of December 31, 2017 and 2016.

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 3) and any other collaborations the Company may enter into.

Multiple-Element Arrangements

The Company recognizes revenue in accordance with 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. 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 commenced when the Company began to deliver the clinical supply of vadadustat to MTPC for use in MTPC's Phase 3 studies of vadadustat in Japan which occurred in the fourth quarter of 2017. Therefore, collaboration revenue prior to the fourth quarter of 2017 is exclusively from the Company's collaborations agreements with Otsuka. The terms of these arrangements 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 these arrangements include: (i) up-front fee, (ii) payments for development services and (iii) payments based on the achievement of certain milestones. Also, under the Otsuka U.S. Agreement, 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 U.S. collaboration with Otsuka. With regards to the MTPC and Otsuka collaboration agreements, the Company recognizes 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 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 revenue 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,* or 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,* or 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 U.S. collaboration with Otsuka as a component of the related expense in the period incurred. During the year ended December 31, 2017, the Company incurred approximately $0.7 million of costs related to the cost-sharing provisions of the Otsuka U.S. Agreement of which approximately $0.2 million are reimbursable by Otsuka and recorded as a reduction to

research and development expense during the year ended December 31, 2017. To the extent product 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.

Research and Development Costs

Research and development costs are expensed as incurred.

Research and development expenses are comprised of costs incurred in providing research and development activities, including salaries and benefits, facilities costs, overhead costs, contract research and development services, and other outside costs. Nonrefundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

External research and development expenses associated with the Company's programs include clinical trial site costs, research compounds and clinical manufacturing costs, costs incurred for consultants and other outside services, such as data management and statistical analysis support, and materials and supplies used in support of the clinical and preclinical programs. Internal costs of the Company's clinical program include salaries, benefits, stock-based compensation, and an allocation of the Company's facility costs. When third-party service providers' billing terms do not coincide with the Company's period-end, the Company is required to make estimates of its obligations to those third parties, including clinical trial and pharmaceutical development costs, contractual services costs and costs for supply of its drug candidates, incurred in a given accounting period and record accruals at the end of the period. The Company bases its estimates on its knowledge of the research and development programs, services performed for the period, past history for related activities and the expected duration of the third-party service contract, where applicable.

Income Taxes

Income taxes are recorded in accordance with FASB Topic 740, *Income Taxes,* or 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. All deferred taxes as of December 31, 2017 and 2016 are classified as noncurrent within the income tax provision (see Note 9).

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, 2017 and 2016, 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 ASC Topic 718, *Compensation—Stock Compensation,* or 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 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. The Company's stock-based awards are comprised of stock options, shares of restricted stock, shares of common stock and warrants. The Company estimates the fair value of options granted using the Black-Scholes option pricing model. The Company uses a blend of its stock price and 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. During 2017, the Company began to estimate its volatility by using a blend of its stock price history for the length of time it has market data for its stock and the historical volatility of similar public companies for the expected term of each grant. The Company is in the product development stage with no product 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 adopted ASU No. 2016-09, *Compensation-Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting,* effective in the first quarter of the year ended December 31, 2017. Prior to adoption, share-based compensation expense was recognized on a straight-line basis, net of estimated forfeitures, such that expense was recognized only for share-based awards that are expected to vest. A forfeiture rate was estimated annually and revised, if necessary, in subsequent periods if actual forfeitures differed from initial estimates. Upon adoption, the Company no longer applies a forfeiture rate and instead will account for forfeitures as they occur.

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. ASC Topic 820, *Fair Value Measurements and Disclosures,* or 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 5). 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, cash equivalents, investments, and accounts receivable are the only financial instruments that potentially subject the Company to concentrations of credit risk. The Company maintains its cash, cash equivalents, and investments with high quality, accredited financial institutions and, accordingly, such funds are subject to minimal credit risk. The Company's investment policy includes guidelines on the quality of the institutions and financial instruments and defines allowable investments that the Company believes minimizes the exposure to concentration of 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.

Accounts receivable represent amounts due from collaboration partners. The Company monitors economic conditions to identify facts or circumstances that may indicate that any of its accounts receivable are at risk of collection.

Net Loss per Share

Basic net loss per share is calculated by dividing net loss 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, warrants, 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. Diluted net income per share is calculated by dividing the net income attributable to common stockholders by the weighted-average shares outstanding for the period, including any dilutive effect from outstanding options, warrants, restricted stock and RSUs using the treasury stock method.

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, 2017 and 2016.

	Useful Life	December 31, 2017	December 31, 2016
		(in thousands)	
Computer equipment and software	3	$ 630	$ 476
Furniture and fixtures	5	800	729
Equipment	7	628	50
Leasehold improvements	Shorter of the useful life or remaining lease term (10 years)	2,582	1,763
Office equipment under capital lease	3	36	36
		4,676	3,054
Less accumulated depreciation		(1,059)	(442)
Net property and equipment		$ 3,617	$ 2,612

Depreciation expense, including expense associated with assets under capital leases, was approximately $616,000, $295,000 and $96,000 for the years ended December 31, 2017, 2016 and 2015, respectively.

3. Strategic Collaborations and Other 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 in Japan and certain other Asian countries, collectively, the MTPC Territory. In addition, the Company will supply vadadustat for both clinical and commercial use in the MTPC Territory, subject to MTPC's option to manufacture commercial drug product in the MTPC Territory.

The Company and MTPC agreed that, instead of including Japanese patients in the Company's global Phase 3 program for vadadustat, MTPC would be the sponsor of a Phase 3 program for vadadustat in Japan. Following consultation with the Japanese Pharmaceuticals and Medical Devices Agency, or the PMDA, MTPC initiated its Phase 3 development program for vadadustat in Japan in the fourth quarter of 2017.

In consideration for the exclusive license and other rights contained in the MTPC Agreement, Japanese patients will not be included in the global Phase 3 program and MTPC will make payments totaling up to $265.0 million, comprised of $20.0 million upfront payment, up to $50.0 million in specified development and regulatory milestones, up to $175.0 million in specified commercial milestones, and $20.0 million for Phase 2 studies in Japanese patients completed by the Company and reimbursable by MTPC, as well as tiered double-digit royalty payments up to 20% on sales of vadadustat in the MTPC Territory.

MTPC is responsible for the costs of the Phase 3 program in Japan and other studies required there, and will make no funding payments for the global Phase 3 program. The Company recently completed its Phase 2 study of vadadustat in non-dialysis dependent, or NDD, Japanese patients and reported top-line data in the third quarter of 2017. The Company also announced top-line data on its Phase 2 study of vadadustat in dialysis-dependent, or DD, Japanese patients in Japan in the first quarter of 2018. The costs of these Phase 2 studies are reimbursable by MTPC. Therefore, of the $40.0 million received by the Company in 2016, $20.0 million related to the upfront payment and the remaining $20.0 million is being applied towards costs already incurred by the Company for the Phase 2 studies. In addition, MTPC will reimburse the Company for costs in excess of $20.0 million to complete the studies. The Company has incurred approximately $19.0 million in Phase 2 costs through December 2017 and anticipates incurring an additional approximately $2.4 million in Phase 2 costs through the end of the studies. As a result, MTPC would be required to reimburse the Company an additional approximately $1.4 million related to the two Phase 2 studies.

MTPC initiated a Phase 3 NDD-CKD study and a Phase 3 DD-CKD study in Japan in the fourth quarter of 2017. Pursuant to the terms of the MTPC Agreement, MTPC is responsible for performing all Phase 3 activities related to the development of vadadustat in the MTPC Territory and has sole responsibility for the commercialization of vadadustat in the MTPC Territory as well as for Medical Affairs (as defined in the MTPC Agreement) in the MTPC Territory. Akebia is responsible for the completion of Phase 2 dosing studies as reimbursed by MTPC, manufacturing and supplying vadadustat for clinical use in the MTPC Territory and, if approved by the FDA, will enter into a supply agreement with MTPC for the commercial supply of vadadustat prior to commercial launch.

The Company and MTPC have established a joint steering committee pursuant to the agreement to oversee development and commercialization of vadadustat in the MTPC 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 MTPC Territory; expiration of marketing or regulatory exclusivity in such country in the MTPC Territory; or ten years after the first commercial sale of vadadustat in such country in the MTPC 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.

MTPC is required to make certain milestone payments to the Company aggregating to approximately $225.0 million upon the achievement of specified development, regulatory and commercial events. More specifically, the Company is eligible to receive up to $10.0 million in development milestone payments, up to $40.0 million in regulatory milestone payments for the first product to achieve the associated event and up to $175.0 million in commercial milestone payments associated with aggregate sales of all products. Additionally, if vadadustat is commercialized, the Company would be entitled to receive tiered royalty payments in the low double digits based on a percentage of net sales. Royalty payments are subject to certain reductions, including upon the introduction of competitive products in certain instances. Royalties are due on a country-by-country basis from the date of first commercial sale of a licensed product in a country until the last to occur of: (i) the expiration of the last to expire valid claim within the intellectual property covering the licensed product, (ii) the expiration of marketing or regulatory exclusivity in such country, or (iii) the tenth anniversary of the first commercial sale of such licensed product in such country. Due to the uncertainty of pharmaceutical development and the high historical failure rates associated with drug development, no milestone or royalty payments may ever be received from MTPC.

In September 2017, the Company and MTPC entered into a new agreement that provided MTPC with an option to access data from the Company's global Phase 3 vadadustat program for payments to the Company of up to $25.0 million.

Revenue Recognition

The Company evaluated the elements of the MTPC Agreement in accordance with the provisions of ASC 605-25. The Company's arrangement with MTPC contains the following deliverables: (i) license under certain of the Company's intellectual property to develop and commercialize vadadustat in the MTPC Territory (the License Deliverable), (ii) clinical supply of vadadustat, (iii) knowledge transfer, (iv) Phase 2 dosing study research services, and (v) rights to future know-how.

The Company has identified two units of accounting in connection with its obligations under the MTPC Agreement. 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. The two units of accounting identified in connection with the Company's obligations under the MTPC Agreement are as follows:

(i) License, Research Services and Clinical Supply Unit of Accounting

The License Deliverable does not have standalone value and does not qualify for separation from the clinical supply of vadadustat. More specifically, the license delivered to MTPC does not provide the contractual right to manufacture vadadustat. MTPC is contractually prohibited from manufacturing any Licensed Product covered by the licenses during clinical trials. Accordingly, MTPC must obtain the clinical trial products from the Company which significantly limits the ability for MTPC to use the license for their intended use on a standalone basis.

The License Deliverable does not have standalone value and does not qualify for separation from the knowledge transfer because MTPC cannot fully utilize the license for its intended purpose without the corresponding information regarding know-how, development data and regulatory materials possessed by the Company.

The License Deliverable does not have standalone value and does not qualify for separation from the Phase 2 dosing study research services because MTPC cannot fully utilize the license for its intended purpose without the performance of the Phase 2 dosing studies. The Phase 2 dosing studies needed to be performed prior to the PMDA approving any Phase 3 study to be performed in the MTPC Territory. Furthermore, MTPC cannot benefit from the Phase 2 dosing studies without the license and the undelivered Phase 3 clinical supply.

The License Deliverable does not have standalone value from the clinical supply, knowledge transfer or Phase 2 studies. As a result, the License Deliverable, clinical supply, knowledge transfer and Phase 2 studies have been combined as a single unit of accounting (the License, Research and Clinical Supply Unit of Accounting)

(ii) Rights to Future Know-How Unit of Accounting

The License, Research and Clinical Supply Unit of Accounting has standalone value and qualifies for separation from the rights to future know how because MTPC can obtain the value of the License, Research and Clinical Supply Unit of Accounting without receipt of any rights to future know how that may be discovered or developed in the future.

The Company has determined that neither VSOE of selling price nor TPE of selling price is available for either of the units of accounting identified at inception of the arrangement with MTPC. 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. The Company developed the BESP for the Rights to Future Know How 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, Research and Clinical Supply Unit of Accounting because the BESP associated with the Rights to Future Know How Unit of Accounting was determined to be immaterial. 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 $20.0 million, (ii) the estimate of the cost for the Phase 2 studies of approximately $21.4 million, and (iii) the cost of all clinical supply provided to MTPC for the Phase 3 studies. No amounts were allocated to the Rights to Know How Unit of Accounting because the associated BESP was determined to be immaterial therefore the arrangement consideration will be allocated to the License, Research Services and Clinical Supply Unit of Accounting.

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, with the exception of one development milestone associated with the near-term progress of the Phase 3 study, 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 non-substantive development milestone will be included in the arrangement consideration, if and when received, and allocated to the License, Research Services and Clinical Unit of Accounting within the arrangement and recognized as revenue when those underlying obligations are satisfied. The total aggregate amount of development milestones is $10.0 million, of which $6.0 million was received in December 2017 and the remaining $4.0 million was invoiced in January 2018, and the total aggregate amount of approval milestones is up to $40.0 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.

Revenue for the fixed and determinable consideration made up of (i) the up-front payment of $20.0 million, (ii) the estimate of the cost for the Phase 2 studies of approximately $21.4 million, (iii) the cost of all clinical supply provided to MTPC for the Phase 3 studies, and (iv) $6.0 million in non-substantive development milestone received in the fourth quarter of 2017 will be recognized using a proportional performance method using the Company's delivery of clinical supply of vadadustat to MTPC for the Phase 3 study as the basis. During the year-end December 31, 2017, the Company recognized revenue totaling $39.7 million with respect to the MTPC agreement. The revenue is classified as collaboration revenue in the accompanying consolidated statement of operations. As of December 31, 2017, there is approximately $7.5 million of short-term deferred revenue and $1.3 million in accounts receivable. There were no asset or liability balances classified as long-term in the consolidated balance sheet as of December 31, 2017.

U.S. Collaboration and License Agreement with Otsuka Pharmaceutical Co. Ltd.

Summary of Agreement

On December 18, 2016, the Company entered into a collaboration and license agreement with Otsuka, or the Otsuka U.S. Agreement. The collaboration is focused on the development and commercialization of vadadustat in the United States. Under the terms of the Otsuka U.S. 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 U.S. 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 U.S. Agreement.

Pursuant to the terms of the Otsuka U.S. 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 with respect to the ongoing PRO_2TECT and $INNO_2VATE$ clinical programs that are necessary through the filing for marketing approval, as well as other studies. Under the Otsuka U.S. 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 U.S. Agreement, the parties jointly conduct, and have equal responsibility for, all medical affairs, commercialization and non-promotional activities pursuant to underlying plans as agreed to by the parties. 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 U.S. Agreement are governed by a joint steering committee, or JSC, formed by an equal number of representatives from the Company and Otsuka. The JSC coordinates and monitors the parties' activities under the collaboration. Among other responsibilities, the JSC manages the overall strategic alignment between the parties, oversees the current global development plan and reviews 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 established a joint development committee, or JDC, which is 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, or 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 U.S. 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 $153.6 million or more, depending on the actual costs incurred toward the vadadustat global development program. 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 therewith, no milestone payments may ever be received from Otsuka.

Under the Otsuka U.S. 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 U.S. Agreement, Otsuka originally had 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). On August 4, 2017, Otsuka agreed to waive its right to exercise the Royalty Conversion Option in advance of its expiration, consequently, Otsuka has no further right to elect to exercise this option.

Unless earlier terminated, the Otsuka U.S. 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 U.S. Agreement in its entirety upon an uncured breach or insolvency on the part of the other party. Otsuka may terminate the Otsuka U.S. 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 for vadadustat. In the event of termination of the Otsuka U.S. Agreement, all rights and licensees granted to Otsuka under the Otsuka U.S. Agreement will automatically terminate and the licenses granted to the Company will become freely sublicensable. In addition, the upfront payment, all development costs and milestone payments received by the Company prior to such termination will not be refunded to Otsuka.

Revenue Recognition

The Company evaluated the elements of the Otsuka US 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 Development Services Deliverable), (iii) rights to future intellectual property (the Future IP Deliverable), and (iv) joint committee services (the Committee Deliverable).

The Company has identified three units of accounting in connection with its obligations under the Otsuka U.S. Agreement. 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 Otsuka U.S. Agreement does not include a general right of return. The three units of accounting identified in connection with the Company's obligations under the Otsuka U.S. Agreement are as follows:

(i) License and Development Services Combined (License Unit of Accounting)

The License Deliverable does not qualify for separation from the 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 marketing 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 Unit of Accounting

The License Deliverable and the Development Services Deliverable qualify for separation from the Future IP Deliverable 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. The Future IP Deliverable qualifies for separation from the Committee Deliverable because the joint committee services have no bearing on the value to be derived from the rights to potential future intellectual property.

(iii) Joint Committee Services Unit of Accounting

The License Deliverable and Development Services Deliverable qualify for separation from the Committee Deliverable 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 Committee Deliverable has standalone value from the rights to Future IP Deliverable 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 Otsuka U.S. Agreement. 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. As of December 31, 2017, the estimate of the cost share payments to be received is $153.6 million or more. 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 $312.4 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 Otsuka U.S. 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 be recorded as revenue upon achievement of the milestone, assuming all other revenue recognition criteria are met.

During the years ended December 31, 2017 and December 31, 2016, the Company recognized revenue totaling approximately $86.0 million and $1.5 million, respectively, with respect to the Otsuka U.S. Agreement. The revenue is classified as collaboration revenue in the accompanying consolidated statement of operations. As of December 31, 2017, there is approximately $99.9 million of deferred revenue related to the Otsuka U.S. Agreement of which $45.3 million is classified as current and $54.6 million is classified as long-term in the accompanying consolidated balance sheet based on the performance period of the underlying obligations. Additionally, as of December 31, 2017, there is approximately $17.3 million in accounts receivable, of which $2.0 million is in unbilled accounts receivable, in the accompanying consolidated balance sheet.

The Company determined that the medical affairs, commercialization and non-promotional activities elements of the Otsuka U.S. 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 success of the activities. Accordingly, the Company is accounting for the joint medical affairs, commercialization and non-promotional activities in accordance with ASC No. 808, *Collaborative Arrangements,* or ASC 808. Additionally, the medical affairs, commercialization and non-promotional activities were not deemed to be deliverables under ASC No. 605-25, *Revenue Recognition–Multiple-Element Arrangements,* or ASC 605-25. As a result, the activities conducted pursuant to the medical affairs, commercialization and non-promotional activities plans will be accounted for as a component of the related expense in the period incurred. During the year ended December 31, 2017, the Company incurred approximately $0.7 million of costs related to the cost-sharing provisions of the Otsuka U.S. Agreement of which approximately $0.2 million are reimbursable by Otsuka and recorded as a reduction to research and development expense during the year ended December 31, 2017.

International Collaboration and License Agreement with Otsuka Pharmaceutical Co. Ltd.

Summary of Agreement

On April 25, 2017, the Company entered into a collaboration and license agreement with Otsuka, or the Otsuka International Agreement. The collaboration is focused on the development and commercialization of vadadustat in Europe, Russia, China, Canada, Australia, the Middle East and certain other territories, collectively, the Otsuka International Territory. Under the terms of the Otsuka International Agreement, the Company will continue to lead the development of vadadustat, including the ongoing global Phase 3 development program. Otsuka has the sole responsibility, at its own cost, for the commercialization of vadadustat in the Otsuka International Territory, subject to the approval by the relevant regulatory authorities.

Under the terms of the Otsuka International Agreement, the Company granted to Otsuka an exclusive, sublicensable license under certain intellectual property controlled by the Company to develop and commercialize vadadustat and products containing or comprising vadadustat in the Otsuka International Territory.

Pursuant to the terms of the Otsuka International Agreement, the Company is responsible for performing all activities related to the development of vadadustat as outlined in the current global development plan; however, the parties may agree to allocate certain responsibilities to Otsuka. The current global development plan encompasses all activities with respect to the ongoing PRO_2TECT and $INNO_2VATE$ program, as well as other studies, through the filing for marketing approval. The current global development plan also includes other derivative and ancillary studies. Under the Otsuka International Agreement, the Company controls and retains final decision-making authority with respect to the development of vadadustat other than with respect to certain development matters specific to the Otsuka International Territory. Per the terms of the Otsuka International Agreement, Otsuka is generally responsible for the conduct of any development activities that may be required for marketing approval in the Otsuka International Territory or otherwise performed with respect to the Otsuka International Territory that are incremental to those included in the current global development plan. 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 International Agreement, Otsuka is to be solely responsible for the conduct of all medical affairs and commercialization activities in the Otsuka International Territory pursuant to underlying plans as reviewed and discussed by the parties. If approved by the relevant jurisdictional regulatory health authorities in the Otsuka International Territory, the Company will provide vadadustat to Otsuka for commercialization pursuant to a separate supply agreement to be negotiated.

The activities under the Otsuka International Agreement are governed by a JSC formed by up to a specified number of representatives from the Company and Otsuka. The JSC coordinates and monitors the parties' activities under the collaboration. Among other responsibilities, the JSC manages the overall strategic alignment between the parties, oversees the current global development plan and reviews the other detailed plans setting forth any other development activities that may be conducted under the arrangement. Additionally, the parties established a JDC which is be comprised of up to a specified number of representatives from the Company and Otsuka. Among other responsibilities, the JDC shares information related to, and reviews and discusses activities and progress under, the current global development plan and any other development that may be conducted pursuant to the collaboration. The Company and Otsuka also established a joint manufacturing committee, or JMC, which is comprised of up to a specified number of representatives from each of the parties. Among other responsibilities, the JMC oversees the manufacturing plan and related manufacturing activities. In support of the potential commercialization of vadadustat, the parties established a JCC which is comprised of up to a specified number of representatives from the Company and Otsuka. Among other responsibilities, the JCC reviews and discusses the activities and progress under the commercialization plan and all other sales and marketing activities. The Company has retained the final decision-making authority with respect to all development matters, other than decisions related to certain development matters specific to the Otsuka International Territory. Otsuka has retained the final decision-making authority with respect to all commercialization matters, other than decisions related to certain marketing matters.

Under the terms of the Otsuka International Agreement, the Company received a $73.0 million up-front, non-refundable, non-creditable cash payment. The Company also received a payment of approximately $0.2 million which represents reimbursement for Otsuka's share of costs previously incurred by the Company in implementing the current global development plan in excess of a specified threshold during the quarter-ended March 31, 2017. Additionally, Otsuka will contribute a percentage of the remaining costs to be incurred under the current global development plan subsequent to March 31, 2017. The Company estimates that Otsuka's funding of the current global development plan costs subsequent to March 31, 2017 will total roughly $163.6 million or more, depending on the actual global development costs incurred. The costs associated with the performance of any mutually agreed upon 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. Otsuka may elect to conduct additional studies of vadadustat in the EU, subject to the Company's right to delay such studies based on its objectives outside the Otsuka International Territory. Otsuka will pay a percentage of the costs of any such studies, and the Company will pay its portion of the costs in the form of a credit against future amounts due to the Company under the Otsuka International Agreement. The costs incurred related to any other development activities, which are pursued solely for obtaining or maintaining marketing approval in the Otsuka International Territory or otherwise performed solely with respect to the Otsuka International Territory that are incremental to the development activities included in the current global development plan, will be borne in their entirety by Otsuka. Otsuka will pay costs incurred with respect to medical affairs and commercialization activities in the Otsuka International Territory.

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 $80.0 million in development milestone payments and up to $52.0 million in regulatory milestone payments for the first product to achieve the associated event. Moreover, the Company is eligible for up to $525.0 million in commercial milestone payments associated with aggregate sales of all products. Additionally, to the extent vadadustat is commercialized, the Company would be entitled to receive tiered royalty payments ranging from the low double digits to the low thirties based on a percentage of net sales. Royalties are due on a country-by-country basis from the date of the first commercial sale of a licensed product in a country until the latest to occur of: (i) the expiration date in such country of the last to expire valid claim within the intellectual property covering the licensed product, (ii) the date of expiration of data or regulatory exclusivity in such country or (iii) the tenth anniversary of the first commercial sale of such licensed product in such country. Due to the uncertainty of pharmaceutical development and the high historical failure rates associated therewith, no milestone or royalty payments may ever be received from Otsuka. There are no cancellation, termination or refund provisions in the Otsuka International Agreement that contain material financial consequences to the Company.

Unless earlier terminated, the Otsuka International Agreement will expire upon the expiration of the royalty term in the last country in the Otsuka International Territory. Either party may terminate the Otsuka International Agreement in its entirety upon an uncured material breach or insolvency on the part of the other party. Otsuka may terminate the Otsuka International Agreement in its entirety or for a specific sub-division of the Otsuka International Territory upon 12 months' prior written notice at any time after the release of the first topline data from either the PRO_2TECT Phase 3 development program or the $INNO_2VATE$ Phase 3 development program, whichever comes first. In the event of termination of the Otsuka International Agreement, all rights and licensees granted to Otsuka under the Otsuka International 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 refund to Otsuka.

Revenue Recognition

The Company has accounted for the Otsuka International Agreement separately from the collaboration arrangement with Otsuka with respect to the U.S. due to the lack of interrelationship and interdependence of the elements and payment terms within each of the contracts as it relates to the respective territories. Accordingly, the Company has applied the guidance in ASC No. 605-25, *Revenue Recognition–Multiple-Element Arrangements,* or ASC 605-25, solely in reference to the terms and conditions of the Otsuka International Agreement, while the collaboration arrangement with Otsuka related to the U.S. has continued to be accounted for as a discrete agreement in its own right. The Company evaluated the Otsuka International Agreement in accordance with the provisions of ASC 605-25. The Company's arrangement with Otsuka related to the Otsuka International Territory contains the following deliverables: (i) license under certain of the Company's intellectual property to develop and commercialize (including the associated packaging) vadadustat and products containing or comprising vadadustat (the License Deliverable), (ii) development services to be performed pursuant to the current global development plan (the Development Services Deliverable), (iii) rights to future intellectual property (the Future IP Deliverable) and (iv) joint committee services (the Committee Deliverable).

The Company has identified three units of accounting in connection with its obligation under the Otsuka International Agreement. Factors considered in making this assessment 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 Otsuka International Agreement does not include a general right of return. The three units of accounting identified in connection with the Company's obligations under the Otsuka International Agreement are as follows:

(i) *License and Development Services Combined (License Unit of Accounting)*

The License Deliverable does not qualify for separation from the 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 marketing 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. Therefore, the License Deliverable does not have standalone value from the Development Services Deliverable. As a result, the License Deliverable and the Development Services Deliverable have been combined as a single unit of accounting (the License Unit of Accounting).

(ii) *Rights to Future Intellectual Property Unit of Accounting*

The License Deliverable and the Development Services Deliverable qualify for separation from the Future IP Deliverable 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. The Future IP Deliverable qualifies for separation from the Committee Deliverable because the Committee Services Deliverable has no bearing on the value to be derived from the rights to potential future intellectual property.

(iii) *Joint Committee Services Unit of Accounting*

The License Deliverable and the Development Services deliverable qualify for separation from the Committee Deliverable because Otsuka can obtain the value of the license using the clinical trial materials implicit in the development service without the joint committee services. The Committee Deliverable qualifies for separation from the Future IP Deliverable because the Committee Deliverable has 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 $73.0 million, (ii) the cost share payment with respect to amounts incurred by the Company during the quarter ended March 31, 2017 of $0.2 million and (iii) an estimate of the cost share payments to be received with respect to amounts incurred by the Company subsequent to March 31, 2017. As of December 31, 2017, the estimate of the cost share payments to be received is approximately $163.6 million. 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 $236.8 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 Otsuka International 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 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.

During the year ended December 31, 2017, the Company recognized revenue totaling approximately $52.3 million with respect to the Otsuka International Agreement. The revenue is classified as collaboration revenue in the accompanying consolidated statement of operations. As of December 31, 2017, there is approximately $70.8 million of deferred revenue related to the Otsuka International Agreement of which $32.1 million is classified as current and $38.7 million is classified as long-term in the accompanying consolidated balance sheet based on the performance period of the underlying obligations. Additionally, as of December 31, 2017, there is approximately $15.6 million in accounts receivable, of which $1.7 million is in unbilled accounts receivable, in the accompanying consolidated balance sheet.

Janssen Pharmaceutica NV Research and License Agreement

Summary of Agreement

On February 9, 2017, the Company entered into a Research and License Agreement, the Janssen Agreement, with Janssen Pharmaceutica NV, or Janssen, a subsidiary of Johnson & Johnson, 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.

Under the terms of the Janssen Agreement, Janssen granted to the Company a license for a three-year research term to conduct research on the HIF compound portfolio, unless the Company elects to extend such research term for up to two additional one-year periods upon payment of an extension fee. During the research term, the Company may designate one or more compounds as candidates for development and commercialization. Once a compound is designated for development and commercialization, the Company will be solely responsible for the development and commercialization of the compound worldwide at its own cost and expense. The Janssen Agreement includes a license to develop and commercialize AKB-5169, a preclinical compound in development as an oral treatment for inflammatory bowel disease, or IBD.

Under the terms of the Janssen Agreement, the Company made an upfront payment of $1.0 million in cash to Janssen and issued a warrant to purchase 509,611 shares of the Company's common stock. 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.

Unless earlier terminated, the Janssen Agreement will expire on a product-by-product and country-by-country basis upon the expiration of the last royalty term, which ends upon the longer of the expiry of the patents licensed under the Janssen Agreement, the expiry of regulatory exclusivity for such product, or 10 years from first commercial sale of such product. The Company may terminate the Janssen Agreement in its entirety or only with respect to a particular licensed compound or product upon 180 days' prior written notice to Janssen. The parties also have customary termination rights, subject to a cure period, in the event of the other party's material breach of the Janssen Agreement or in the event of certain additional circumstances.

As discussed above, 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 Warrant and the shares issuable upon exercise of the Warrant will be sold and issued without registration under the Securities Act of 1933, or the Securities Act. The Company recorded the fair value of the warrant in the amount of $3.4 million to additional paid in capital and research and development expense in March 2017.

Vifor Pharma License Agreement

Summary of License Agreement

On May 12, 2017, the Company entered into a License Agreement, or the Vifor Agreement, with Vifor (International) Ltd., or Vifor Pharma, pursuant to which the Company will grant Vifor Pharma an exclusive license to sell vadadustat solely to Fresenius Kidney Care Group LLC, or FKC, an affiliate of Fresenius Medical Care North America, in the United States.

The parties' rights under the Vifor Agreement are conditioned upon the approval of vadadustat for DD-CKD patients by the FDA, inclusion of vadadustat in a bundled reimbursement model, and payment by Vifor Pharma of a $20.0 million milestone upon the occurrence of these two events. The Vifor Agreement is structured as a profit share arrangement between the Company and Vifor Pharma in which the Company will receive a majority of the profit from Vifor Pharma's sales of vadadustat to FKC in the United States. The Company will share the milestone payment and the revenue from the profit share with Otsuka pursuant to the Otsuka U.S Agreement. The Company retains all rights to commercialize vadadustat for use in the NDD-CKD market and in other dialysis organizations in the United States, which will be done in collaboration with Otsuka following FDA approval.

Prior to FDA approval of vadadustat, the Company and Vifor Pharma will enter into a commercial supply agreement for vadadustat pursuant to which the Company will supply all of Vifor Pharma's requirements for vadadustat in the United States. In addition, Vifor Pharma will enter into a supply agreement with FKC that will govern the terms pursuant to which Vifor Pharma will supply vadadustat to FKC for use in patients at its dialysis centers. During the term of the Vifor Agreement, Vifor Pharma will not sell to FKC or its affiliates any HIF product that competes with vadadustat in the United States.

Unless earlier terminated, the Vifor Agreement will expire upon the later of the expiration of all patents that claim or cover vadadustat, or expiration of data or regulatory exclusivity for vadadustat in the United States. Vifor Pharma may terminate the Vifor Agreement in its entirety upon 12 months' prior written notice after the release of the first topline data in the vadadustat global Phase 3 program for dialysis-dependent CKD patients. Either party may terminate the Vifor Agreement in the event of the other party's uncured material breach. The Company may also terminate the Vifor Agreement upon the occurrence of other events, such as for specific violations of the Vifor Agreement or if there are changes in Vifor Pharma's relationship with FKC.

Investment Agreement

In connection with the Vifor Agreement, in May 2017, the Company and Vifor Pharma entered into an investment agreement, the Investment Agreement, pursuant to which the Company sold an aggregate of 3,571,429 shares of common stock, the Shares, par value $0.00001 per share, to Vifor Pharma at a price per share of $14.00 for a total of $50.0 million dollars. The amount representing the premium over the closing stock price of $12.69 on the date of the transaction, totaling $4.7 million, was determined by the Company to represent consideration related to the Vifor Agreement. As the parties' rights under the Vifor Agreement are conditioned upon (a) the approval of vadadustat for DD-CKD patients by the FDA; (b) inclusion of vadadustat in a bundled reimbursement model; and (c) payment by Vifor Pharma of a $20.0 million milestone upon the occurrence of these two events, in accordance with ASC 605, the Company cannot currently determine the extent of its responsibility to supply all of Vifor Pharma's requirements for vadadustat in the United States. Accordingly, the $4.7 million is recorded as deferred revenue in the accompanying consolidated balance sheets. Upon the satisfaction of the aforementioned conditions, revenue will be recognized as the Company supplies vadadustat to Vifor Pharma using a proportional performance method.

Vifor Pharma has agreed to a lock-up restriction such that it agrees not to sell its shares for a period of time following the effective date of the Investment Agreement as well as a customary standstill agreement. In addition, the Investment Agreement contains voting agreements made by Vifor Pharma with respect to the Shares. The Shares have not been registered pursuant to Securities Act of 1933, the "Act", and were issued and sold in reliance upon the exemption from registration contained in Section 4(a)(2) of the Act and Rule 506 promulgated thereunder.

4. Available for Sale Securities

Available for sale securities at December 31, 2017 and 2016 consist of the following:

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
		(in thousands)		
December 31, 2017				
Cash and cash equivalents	$ 70,156	$ —	$ —	$ 70,156
Available for sale securities:				
Certificates of deposit	$ 14,117	—	—	$ 14,117
U.S. government debt securities	175,155	—	(352)	174,803
Corporate debt securities	58,806	—	(90)	58,716
Total available for sale securities	$ 248,078	$ —	$ (442)	$ 247,636
Total cash, cash equivalents, and available for sale securities	$ 318,234	$ —	$ (442)	$ 317,792

	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

The estimated fair value of the Company's available for sale securities balance at December 31, 2017, by contractual maturity, is as follows:

Due in one year or less	$ 217,884
Due after one year	29,752
Total available for sale securities	$ 247,636

There were no realized gains or losses on available for sale securities for the years ended December 31, 2017 or 2016. There were three U.S. government debt securities that had been in an unrealized loss position for more than 12 months as of December 31, 2017 with an aggregate unrealized loss on these securities of $9,000 and fair value of $4.0 million. There were no available for sale securities that had been in an unrealized position for more than 12 months as of December 31, 2016. There were 57 securities in a loss position for less than 12 months at December 31, 2017 with an aggregate unrealized loss on these securities of $433,000 and fair value of $229.5 million. There were 27 securities in a loss position for less than 12 months at December 31, 2016 with an aggregate unrealized loss on these securities of $40,000 and fair value of $60.3 million. The Company considered the decline in the market value of these securities to be primarily attributable to current economic conditions. The contractual terms of these securities do not permit the issuer to settle the securities at a price less than the amortized cost basis of the investment. As it was not more likely than not that the Company would be required to sell these securities before the recovery of their amortized cost basis, which may be at maturity, the Company did not consider these investments to be other-than-temporarily impaired as of December 31, 2017.

5. 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 December 31, 2017 and December 31, 2016 are summarized below:

	Fair Value Measurements Using			
	Level 1	Level 2	Level 3	Total
	(in thousands)			
December 31, 2017				
Assets:				
Cash and cash equivalents	$ 70,156	$ —	$ —	$ 70,156
Certificates of deposit	—	14,117	—	14,117
U.S. government debt securities	—	174,803	—	174,803
Corporate debt securities	—	58,716	—	58,716
	$ 70,156	$ 247,636	$ —	$ 317,792

	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

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, 2017 and December 31, 2016.

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.

6. Accrued Expenses

Accrued expenses are as follows:

	December 31, 2017	December 31, 2016
	(in thousands)	
Accrued clinical	$ 43,297	$ 23,643
Accrued bonus	3,388	2,995
Income tax payable	987	—
Professional fees	808	539
Accrued vacation	797	513
Accrued payroll	795	596
Accrued severance	—	29
Other	2,369	1,946
Total accrued expenses	$ 52,441	$ 30,261

7. Warrant

In connection with the Janssen Agreement, in February 2017 the Company issued a warrant to purchase 509,611 shares of the Company's common stock at an exercise price of $9.81 per share. The warrant was fully vested upon issuance and exercisable in whole or in part, at any time prior to the fifth anniversary of the date of issuance. The warrant satisfied the equity classification criteria of ASC 815, and is therefore classified as an equity instrument. The fair value at issuance of $3.4 million was calculated using the Black-Scholes option pricing model and was charged to research and development expense as it represented consideration for a license for which the underlying intellectual property was deemed to have no alternative future use. As of December 31, 2017, the warrant remains outstanding and expires on February 9, 2022.

8. Stockholders' Equity

Authorized and Outstanding Capital Stock

As of December 31, 2017, the authorized capital stock of the Company included 175,000,000 shares of common stock, par value $0.00001 per share, of which 47,612,619 and 38,615,709 shares were issued and outstanding at December 31, 2017 and 2016, respectively; and 25,000,000 shares of undesignated preferred stock, par value $0.00001 per share, of which 0 shares were issued and outstanding at December 31, 2017 and December 31, 2016.

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.

At-the-Market Facility

In May 2016, the Company established an at-the-market equity offering program pursuant to which it was able to offer and sell up to $75.0 million its common stock at the then current market prices from time to time. In September 2016, the Company commenced sales under this program. During the years ended December 31, 2017 and 2016, the Company sold 465,615 and 615,293 shares of common stock, respectively, under this program with net proceeds (after deducting commissions and other offering expenses) of $6.4 million and $5.7 million, respectively.

From January 1, 2018 through March 12, 2018, the Company sold 694,306 shares of common stock under the at-the-market offering program with net proceeds (after deducting commissions and other offering expenses) of $10.5 million.

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 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 Rule 5635(c)(4), did not require shareholder approval (the "2016 Inducement Award Program"). In 2017, the Company authorized the issuance of up to 700,000 shares for new hires under the 2016 Inducement Award Program, of which 525,500 stock options were granted during the year. At December 31, 2017, 508,500 stock options granted in 2017 under the 2016 Inducement Award Program remain eligible to vest.

The 2014 Plan allows for the granting of stock options, stock appreciation rights (SARs), restricted stock, unrestricted stock, restricted stock units (RSUs), 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, 2017, the Company granted 719,400 stock options to employees under the 2014 Plan, 525,500 stock options to employees under the 2016 Inducement Award Program, 449,900 restricted stock units (RSUs) to employees under the 2014 Plan, and 87,500 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 eighty-five percent (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, 2017	December 31, 2016
Common stock options and RSU's outstanding (1)	4,388,752	3,579,694
Shares available for issuance under the 2014 Plan (2)	1,790,600	1,140,328
Warrant to purchase common stock	509,611	—
Shares available for issuance under the ESPP (3)	652,290	803,105
Total	7,341,253	5,523,127

(1) Includes awards granted under the 2014 Plan and the 2016 Inducement Award Program.

(2) On January 1, 2018, January 1, 2017 and January 1, 2016, the shares reserved for future grants under the 2014 Plan increased by 1,575,329, 1,265,863 and 986,800 shares, respectively, pursuant to the 2014 Plan Evergreen Provision. On December 19, 2017, the Company's Board of Directors approved 750,000 shares to become available for issuance effective January 1, 2018 under the 2016 Inducement Award Program. As these shares are not available for issuance as of year-end, they have been excluded from the table above.

(3) On February 28, 2017 and February 28, 2016, the shares reserved for future issuance under the ESPP increased by 0 and 273,404 shares, respectively, pursuant to the ESPP Evergreen Provision.

Stock-Based Compensation

Stock Options

On February 21, 2017, as part of the Company's annual grant of equity, the Company issued 719,400 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 installments beginning in the thirteenth month after the initial vesting commencement date or 12 equal quarterly installments beginning on the first day of each calendar quarter 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 $6.5 million and $4.7 million of stock-based compensation expense related to stock options during 2017 and 2016, respectively.

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,		
	2017	2016	2015
Risk-free interest rate	1.81% - 2.27%	1.16% - 2.03%	1.44% - 1.95%
Dividend yield	0.00%	0.00%	0.00%
Volatility	78.57% - 85.81%	64.78% - 82.40%	62.47% - 81.25%
Expected term (years)	5.51 - 6.25	5.51 - 6.25	5.51 - 6.25

The following table summarizes the Company's stock option activity for the year ended December 31, 2017:

	Shares	Weighted-Average Exercise Price	Weighted-Average Contractual Life (in years)	Aggregate Intrinsic Value
Outstanding, December 31, 2016	3,148,006	$ 8.93		$ 10,437,947
Granted	1,332,400	$ 11.95		
Exercised	(291,439)	$ 5.28		$ 2,689,563
Forfeited	(528,953)	$ 14.80		$ 1,502,894
Expired/cancelled	—			
Outstanding, December 31, 2017	3,660,014	$ 9.47	8.00	$ 21,932,858
Options exercisable, December 31, 2017	1,574,788	$ 7.62	6.85	$ 12,971,099
Expected to vest, December 31, 2017	2,085,226	$ 10.88		

The weighted-average grant date fair values of options granted in the years ended December 31, 2017, 2016, and 2015 were $8.47, $5.22, and $6.07 per share, respectively. The total intrinsic value of options exercised during the years ended December 31, 2017, 2016, and 2015 were $2.7 million, $0.6 million, and $2.0 million, respectively. The fair value of options that vested during the years ended December 31, 2017, 2016, and 2015 were $5.6 million, $4.6 million, and $3.2 million, respectively. As of December 31, 2017, there was approximately $13.0 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 2.72 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 the vesting commencement day was 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 had a requisite service period that was complete upon grant. The remainder of the awards of restricted stock had a requisite service period of four years whereby the award vested 25% on the one year anniversary of 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. The Company records stock-based compensation expense for restricted stock awards based on the grant date fair value for employees and the reporting date and upon vesting fair value for non-employees. The fair value of the award is considered the intrinsic value as of each measurement date.

Compensation expense related to the restricted stock awards is being recognized over the associated requisite service period which commenced on March 25, 2014. The Company recorded approximately $0.2 million and $0.3 million of stock-based compensation expense related to restricted stock during 2017 and 2016, respectively, of which approximately $132,154 and $3,000 was as a result of mark to market adjustments related to non-employees.

The following table summarizes the Company's restricted stock activity for the year ended December 31, 2017:

	Shares		Weighted-Average Grant Date Fair Value
Restricted shares as of December 31, 2016	92,972	$	8.08
Granted	—		
Vested	(90,566)	$	8.56
Forfeited	(2,406)	$	7.42
Restricted shares as of December 31, 2017	-	$	-

As of December 31, 2017, there was approximately $0 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.

Restricted Stock Units

On February 21, 2017, as part of the Company's annual grant of equity, the Company issued 423,650 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 either the first or the third anniversary of the grant date, subject, in each case, to the individual's continued service through the applicable vesting date. The expense recognized for these awards is based on the grant date fair value of the Company's common stock multiplied by the number of units granted and recognized on a straight-line basis over the vesting period. The Company recorded approximately $2.0 million and $0.8 million of stock-based compensation expense related to the RSUs in 2017 and 2016, respectively.

A following table summarizes the Company's RSU activity for the year ended December 31, 2017:

	Shares		Weighted-Average Grant Date Fair Value
Unvested balance, December 31, 2016	431,688	$	7.96
Granted	449,900	$	10.34
Vested	(26,000)	$	7.70
Forfeited	(126,850)	$	8.96
Outstanding, December 31, 2017	728,738	$	9.26

As of December 31, 2017, there was approximately $4.0 million of unrecognized compensation cost related to RSUs, which is expected to be recognized over a weighted average period of 1.91 years.

Employee Stock Purchase Plan

The first offering period under the ESPP opened on January 2, 2015. The Company issued 44,789 shares issued during the year ended December 31, 2017. The Company recorded approximately $0.2 million and $0.1 million of stock-based compensation expense related to the ESPP during 2017 and 2016, respectively.

Compensation Expense Summary

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

	Years ended December 31,		
	2017	2016	2015
	(in thousands)		
Research and development	$ 6,496	$ 2,136	$ 2,079
General and administrative	5,784	3,689	2,635
Total	$ 12,280	$ 5,825	$ 4,714

Compensation expense by type of award:

	Years ended December 31,		
	2017	2016	2015
	(in thousands)		
Stock options	$ 6,512	$ 4,674	$ 3,660
Restricted stock	158	266	909
Restricted stock units	2,021	780	62
Employee stock purchase plan	176	105	83
Warrant	3,413	—	—
Total	$ 12,280	$ 5,825	$ 4,714

9. Income Taxes

For the year ended December 31, 2017, the Company has taxable income primarily due to timing differences. The losses are fully offset with available NOLs for regular federal and state tax purposes. The Company does have a tax liability for Alternative Minimum Tax in 2017, however due to tax reform, the amount that will be paid this year is fully refundable through 2021 and thus the net result is that the Company recorded an income tax receivable rather than a tax expense for the year ended December 31, 2017. The Company recorded a receivable of approximately $1.0 million and a payable of approximately $1.0 million for the Alternative Minimum Tax which is included in other assets and accrued expenses, respectively, in the accompanying consolidated balance sheets as of December 31, 2017. The Company has recorded a full valuation allowance on its deferred tax assets and thus, for the year ended December 31, 2017 there is no deferred tax expense recorded. For the years ended December 31, 2016 and 2015, there was no current or deferred tax expense recorded 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,		
	2017	2016	2015
Federal tax at statutory rate	34.0%	34.0%	34.0%
State and local tax at statutory rate	3.8	1.4	3.0
Research and development tax credits	11.9	6.4	0.4
Equity compensation	(0.6)	(0.2)	(0.6)
Alternative minimum tax	(1.3)	—	—
Change in valuation allowance	6.9	(41.6)	(36.8)
Impact of US tax reform	(54.7)	—	—
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 decreased by approximately $4.9 million and increased by approximately $56.4 million, during the years ended December 31, 2017 and 2016. Significant components of the Company's deferred tax assets and liabilities are as follows:

	December 31,	
	2017	2016
	(in thousands)	
Deferred tax assets:		
Accrued expenses	$ 4,305	$ 2,170
Deferred revenue	32,093	12,157
Intangible assets	509	449
Restricted stock	—	45
Non-qualified stock options	3,129	2,963
Research and development credits	25,322	10,510
Net operating loss carryforward	42,335	84,372
Other	600	326
Total deferred tax assets	108,293	112,992
Less valuation allowance	(108,112)	(112,986)
Total deferred tax assets, net of valuation allowance	181	6
Deferred tax liabilities:		
Fixed assets	(181)	(6)
Total deferred tax liabilities	(181)	(6)
Net deferred tax asset	$ —	$ —

At December 31, 2017 and December 31, 2016, the Company has approximately $0.8 million (after amortization of $1.1 million) and $0.9 million (after amortization of $1.0 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, 2017 and 2016, the Company has approximately $179.7 million and $234.5 million, respectively, of federal net operating loss (NOL) carry-forwards which expire through 2036. Additionally, at December 31, 2017 and 2016, the Company has approximately $74.6 million and $103.9 million, respectively, of state net operating loss (NOL) carry-forwards which expire through 2036. As a result of the adoption of ASU 2016-09 for the year ended December 31, 2017, the benefits of tax deductions related to equity compensation in excess of book compensation expense that were previously suspended are now recognized for financial statement purposes. To record this tax benefit, both the NOL deferred tax asset and valuation allowance increased by $1.3 million, with a net zero tax impact recorded directly to retained earnings. For comparison purposes, the 2016 NOL deferred tax asset above (prior to the adoption of ASU 2016-09) does not include the benefit of these tax deductions. The Company also has approximately $25.7 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 2037, 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, two of which resulted in a change in control and limitations on the deductibility of existing NOLs at the dates of change of control. As of December 31, 2016, there were $170.0 million unlimited NOLs available to offset taxable income in future years, which allowed for the complete offset of taxable income for the year ended December 31, 2017.

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, 2017, 2016 and 2015, 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 2014 through 2016 tax years remain open and subject to examination by federal and state taxing authorities. However, federal and state net operating losses from 2009 through 2016 are subject to review by taxing authorities in the year utilized.

The Tax Cuts and Jobs Act (the Act), which was signed on December 22, 2017, makes significant change in U.S. tax law including a reduction in the corporate tax rates to 21% starting in 2018. The legislation reduced the U.S. corporate tax rate from the current rate of 35% to 21%for tax years beginning after December 31, 2017. As a result of the enacted law, the Company was required to revalue deferred tax assets and liabilities existing as of December 31, 2017 from the 35% federal rate in effect through the end of 2017, to the new 21% rate. As a result of the change in law, the Company recorded a $43.0 million reduction in the deferred tax asset and corresponding valuation allowance.

In accordance with SAB 118, we have determined that our deferred tax asset value and associated valuation allowance reduction is a provisional amount and a reasonable estimate at December 31, 2017. The final impact may differ from this provisional amount due to, among other things, changes in interpretations and assumptions we have made thus far and the issuance of additional regulatory or other guidance. We expect to complete the final impact within the measurement period.

10. 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 under the initial base rent was approximately $242,000 and is subject to annual rent escalations. In addition to such annual rent escalations, base rent payments for a portion of said premises commenced on 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 $70,526 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 with respect to the lab space expires on November 30, 2021, 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 in the form of a letter of credit and is included in other assets in the Company's consolidated balance sheets as of December 31, 2017 and December 31, 2016.

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 consolidated balance sheets as of December 31, 2017 and December 31, 2016.

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 $0.3 million. The total security deposit in connection with the Sublease of $21,432 is included in other current assets and other liabilities in the Company's consolidated balance sheets as of December 31, 2017 and December 31, 2016.

At December 31, 2017, 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
		(in thousands)	
2018	$ 3,579	$ 257	$ 3,322
2019	3,626	—	$ 3,626
2020	3,675	—	$ 3,675
2021	3,684	—	$ 3,684
2022	3,307	—	$ 3,307
Thereafter	12,573	—	$ 12,573
Total	$ 30,444	$ 257	$ 30,187

The Company recorded approximately $3.2 million and $2.5 million in rent expense for the years ended December 31, 2017 and 2016, respectively.

Under the Company's agreement with IQVIA, formerly known as Quintiles IMS, to provide CRO services for the PRO_2TECT and $INNO_2VATE$ programs, the total remaining contract costs as of December 31, 2017 were approximately $276.4 million. The estimated period of performance for the committed work with IQVIA is through the first quarter of 2020. The Company contracts with various other organizations to conduct research and development activities with remaining contract costs to the Company of approximately $52.4 million at December 31, 2017. 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.

The Company filed an opposition in Europe against FibroGen, Inc.'s, or FibroGen's, European Patent No. 1463823, or the '823 EP Patent, and 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 two to three 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 JP Patent, which is the Japanese counterpart to the '823 EP 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'131 JP 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 EP Patent and '131 JP Patents. In the event FibroGen were to obtain such a patent in the United States, the Company may decide to challenge the patent as we have 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. 2322155, or the '155 EP Patent, 1633333, or the '333 EP patent, and 2322153, or the '153 EP Patent requesting the patents be revoked in their entirety. These related patents claim, among other things, various compounds that either stabilize HIFα 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 the Company does not believe these patents will prevent us from commercializing vadadustat for the treatment of anemia secondary to CKD, the Company filed these oppositions to provide us and our collaborators with maximum flexibility for developing vadadustat and the Company's pipeline of HIF-PHIs.

Oppositions to the '155 EP Patent and the '153 EP Patent were also filed by Glaxo Group Limited, or Glaxo, and by Bayer Intellectual Property GmbH, Bayer Pharma Aktiengesellschaft, and Bayer Animal Health GmbH, or collectively Bayer.

With regards to the opposition that we filed in Europe against the '333 EP patent, an oral proceeding took place on 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. On December 9, 2016, FibroGen filed a notice to appeal the decision to revoke the '333 EP Patent.

In oral proceedings held on May 29, 2017 regarding the ‘155 EP Patent, the European Opposition Division ruled that the '155 EP Patent as granted did not meet the requirements for patentability under the European Patent Convention and, therefore, revoked the patent in its entirety. FibroGen filed a notice to appeal the decision to revoke the ’155 EP Patent on May 29, 2017.

Subsequently, in related oral proceedings held on May 31, 2017 and June 1, 2017 for the '153 EP Patent, the European Opposition Division maintained the patent after FibroGen significantly narrowed the claims to an indication for which vadadustat is not intended to be developed. We and Glaxo separately filed notices to appeal the decision to maintain the ’153 EP Patent on November 9, 2017. Bayer filed a notice to appeal the decision on November 14, 2017.

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.

11. 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, $0.2 million and $0.1 million were made during the years ended December 31, 2017, 2016 and 2015, respectively.

12. Net Loss per Share

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,		
	2017	2016	2015
Warrants	509,611	—	—
Outstanding stock options	3,660,014	3,148,006	2,206,635
Unvested restricted stock	—	92,972	216,716
Unvested restricted stock units	728,738	431,688	24,425
Total	4,898,363	3,672,666	2,447,776

13. Quarterly Results (unaudited)

	Three Months Ended			
	March 31, 2017	June 30, 2017	September 30, 2017	December 31, 2017
	(in thousands, except per share data) (unaudited)			
Collaboration revenue	$ 20,865	$ 28,520	$ 41,283	$ 87,316
Operating expenses	$ 65,837	$ 50,656	$ 65,459	$ 75,949
Loss from operations	$ (44,972)	$ (22,136)	$ (24,176)	$ 11,367
Other income, net	$ 429	$ 618	$ 1,042	$ 914
Net (loss)/income	$ (44,543)	$ (21,518)	$ (23,134)	$ 12,281
Net (loss)/income per share:				
basic	$ (1.15)	$ (0.53)	$ (0.49)	$ 0.26
diluted	$ (1.15)	$ (0.53)	$ (0.49)	$ 0.25
Weighted-average number of common shares:				
basic	38,759,221	40,819,957	46,938,618	47,353,166
diluted	38,759,221	40,819,957	46,938,618	49,719,548

	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 —basic and diluted	$ (0.70)	$ (0.95)	$ (0.96)	$ (0.99)

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

None.

Item 9A. 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) and 15d-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 I*nternal Control - Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission, or COSO. Based on the assessment, management has concluded that our internal control over financial reporting as of December 31, 2017 was effective 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 Exchange Act 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, 2017, 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 Exchange

Act. 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, 2017, our disclosure controls and procedures were effective at the reasonable assurance level.

Changes in Internal Control over Financial Reporting

During the second quarter of fiscal year 2017, we identified and disclosed a material weakness in our internal control over financial reporting resulting from inadequate control over expense recognition of certain cash advance payments made to one of our contract research organizations supporting our global Phase 3 program for vadadustat. Specifically, we did not have adequate controls in place to properly determine the portion of the cash advance payments that should be recorded as an expense in the period and the portion that should be recorded as a prepaid expense. In addition, the amount of revenue recognized pursuant to certain of our collaboration agreements was consequently affected, as such revenue is recognized based on the percentage of expense incurred on the total of the expected cost of the global Phase 3 program for vadadustat. To remediate the material weakness described above, we have: (i) added additional resources, (ii) designed and implemented controls, and (iii) enhanced and revised the design of existing controls and procedures to properly account for certain research and development expenses, primarily the portion of the cash advance payments that should be recorded as an expense in the period and the portion that should be recorded as a prepaid expense.

During the fourth quarter of fiscal year 2017, we successfully completed the testing necessary to ascertain that the applicable controls are effective and operating as designed. As a result, we have concluded that the material weakness has been remediated.

Except as noted above, there have been no changes in the Company's internal control over financial reporting during the fourth quarter of 2017, as such term is defined in Rules 13a-15(f) and 15(d)-15(f) promulgated under the Exchange Act, 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 12, 2018, Akebia announced its financial results for the quarter ended December 31, 2017 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

Item 10. Director, Executive Officers and Corporate Governance

The information required by this Item 10 will be included in our Definitive Proxy Statement to be filed with the Securities and Exchange Commission, or SEC, with respect to our 2018 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 11. Executive Compensation

The information required by this Item 11 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2018 Annual Meeting of Stockholders and is incorporated herein by reference.

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

The information required by this Item 12 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2018 Annual Meeting of Stockholders and is incorporated herein by reference.

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

The information required by this Item 13 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2018 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 14. Principal Accountant Fees and Services

The information required by this Item 14 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2018 Annual Meeting of Stockholders and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules

(a) Documents filed as part of this Annual Report on Form 10-K.

(1) Consolidated 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 below are filed as part of this Annual Report on Form 10-K.

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	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)
4.3#	Common Stock Purchase Warrant between Akebia Therapeutics, Inc. and Janssen Pharmaceutica NV, dated February 9, 2017 (incorporated by reference to exhibit 4.1 to the Company's Quarterly Report on Form 10-Q, filed on May 9, 2017)
4.4#	Investment Agreement between Akebia Therapeutics, Inc. and Vifor (International) Ltd., dated May 12, 2017 (incorporated by reference to exhibit 4.1 to the Company's Quarterly Report on Form 10-Q, filed on August 8, 2017)
4.5*	Amendment No. 1 to Fourth Amended and Restated Investors' Rights Agreement, dated June 28, 2017
10.1*	Form of Director and Officer Indemnification Agreement
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*	Fourth Amendment to Office Lease Agreement Between CLPF-Cambridge Science Center, LLC and Akebia Therapeutics, Inc., dated May 1, 2017
10.7†	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)
10.8†	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)
10.9†	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)
10.10†	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)
10.11†	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)
10.12†	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)
10.13*	Non-Employee Director Compensation Program
10.14†	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)
10.15†	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)
10.16†	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)
10.17†	Cash Incentive Plan (incorporated by reference to exhibit 10.31 to the Company's Registration Statement on Form S-1/A (333-193969),

Exhibit Number	Description of Exhibit
	filed on March 4, 2014)
10.18*†	Form of Restricted Stock Unit Award Agreement under 2014 Incentive Plan
10.19†	Form of Officer Inducement Award Non-Statutory Stock Option Agreement (incorporated by reference to exhibit 4.4 to the Company's Registration Statement on Form S-8 (333-222728), filed on January 26, 2018)
10.20†	Form of Inducement Award Non-Statutory Stock Option Agreement for non-officers (incorporated by reference to exhibit 4.5 to the Company's Registration Statement on Form S-8 (333-222728), filed on January 26, 2018)
10.21#	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)
10.22#	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)
10.23#	Letter Agreement between Akebia Therapeutics, Inc. and Mitsubishi Tanabe Pharma Corporation, dated September 26, 2017 (incorporated by reference to exhibit 10.1 to the Company's Quarterly Report on Form 10-Q, filed on November 8, 2017)
10.24#	Collaboration and License Agreement, between Akebia Therapeutics, Inc. and Otsuka Pharmaceutical Co. Ltd., dated December 18, 2016 (incorporated by reference to exhibit 10.26 to the Company's 10-K for the year ending December 31, 2016 and filed on March 6, 2017)
10.25#	Collaboration and License Agreement between Akebia Therapeutics, Inc. and Otsuka Pharmaceutical Co. Ltd., dated April 25, 2017 (incorporated by reference to exhibit 10.1 to the Company's Quarterly Report on Form 10-Q, filed on August 8, 2017)
10.26#	Research and License Agreement between Akebia Therapeutics, Inc. and Janssen Pharmaceutica NV, dated February 9, 2017 (incorporated by reference to exhibit 10.1 to the Company's Quarterly Report on Form 10-Q, filed on May 9, 2017)
10.27#	License Agreement between Akebia Therapeutics, Inc. and Vifor (International) Ltd., dated May 12, 2017 (incorporated by reference to exhibit 10.2 to the Company's Quarterly Report on Form 10-Q, filed on August 8, 2017)
10.28*†	Offer Letter to Rita Jain, dated April 28, 2017
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 12, 2018 (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

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) 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 12, 2018

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

Pursuant to the requirements of the Securities 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 12, 2018

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

Date: March 12, 2018

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

Date: March 12, 2018

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

Date: March 12, 2018

By: /s/ Duane Nash
Duane Nash
Director

Date: March 12, 2018

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

Date: March 12, 2018

By: /s/ Maxine Gowen
Maxine Gowen
Director

Date: March 12, 2018

By: /s/ Michael D. Clayman
Michael D. Clayman
Director

Date: March 12, 2018

By: /s/ Ronald C. Renaud, Jr.
Ronald C. Renaud, Jr.
Director

Date: March 12, 2018

By: /s/ Scott A. Canute
Scott A. Canute
Director

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statement (Form S-3 No. 333-211175) of Akebia Therapeutics, Inc.,

(2) Registration Statement (Form S-3 No. 333-203206) of Akebia Therapeutics, Inc.,

(3) Registration Statement (Form S-8 No. 333-196748) pertaining to the Amended and Restated 2008 Equity Incentive Plan, the 2014 Incentive Plan, and the 2014 Employee Stock Purchase Plan of Akebia Therapeutics, Inc.,

(4) Registration Statement (Form S-8 No. 333-209469) pertaining to the 2014 Incentive Plan and the 2014 Employee Stock Purchase Plan of Akebia Therapeutics, Inc.,

(5) Registration Statement (Form S-8 No. 333-216475) pertaining to the 2014 Incentive Plan and the 2016 Inducement Award Program of Akebia Therapeutics, Inc., and

(6) Registration Statement (Form S-8 No. 333-222728) pertaining to the 2014 Incentive Plan and the 2016 Inducement Award Program of Akebia Therapeutics, Inc.,

of our report dated March 12, 2018, with respect to the consolidated financial statements of Akebia Therapeutics, Inc. included in this Annual Report (Form 10-K) for the year ended December 31, 2017.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 12, 2018

Exhibit 31.1

CERTIFICATION PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, John P. Butler, certify that:

1. I have reviewed this Annual Report on Form 10-K of Akebia Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the Audit Committee of the registrant's Board of Directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 12, 2018

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

Exhibit 31.2

CERTIFICATION PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Jason A. Amello, certify that:

1. I have reviewed this Annual Report on Form 10-K of Akebia Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the Audit Committee of the registrant's Board of Directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 12, 2018

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

Exhibit 32.1

CERTIFICATION PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002 (18 U.S.C. Section 1350

In connection with the accompanying Annual Report of Akebia Therapeutics, Inc. (the Company) on Form 10-K for the fiscal year ended December 31, 2017 (the Report), I, John P. Butler, as Chief Executive Officer and President of the Company, and I, Jason A. Amello, as Senior Vice President, Chief Financial Officer and Treasurer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that:

1. The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

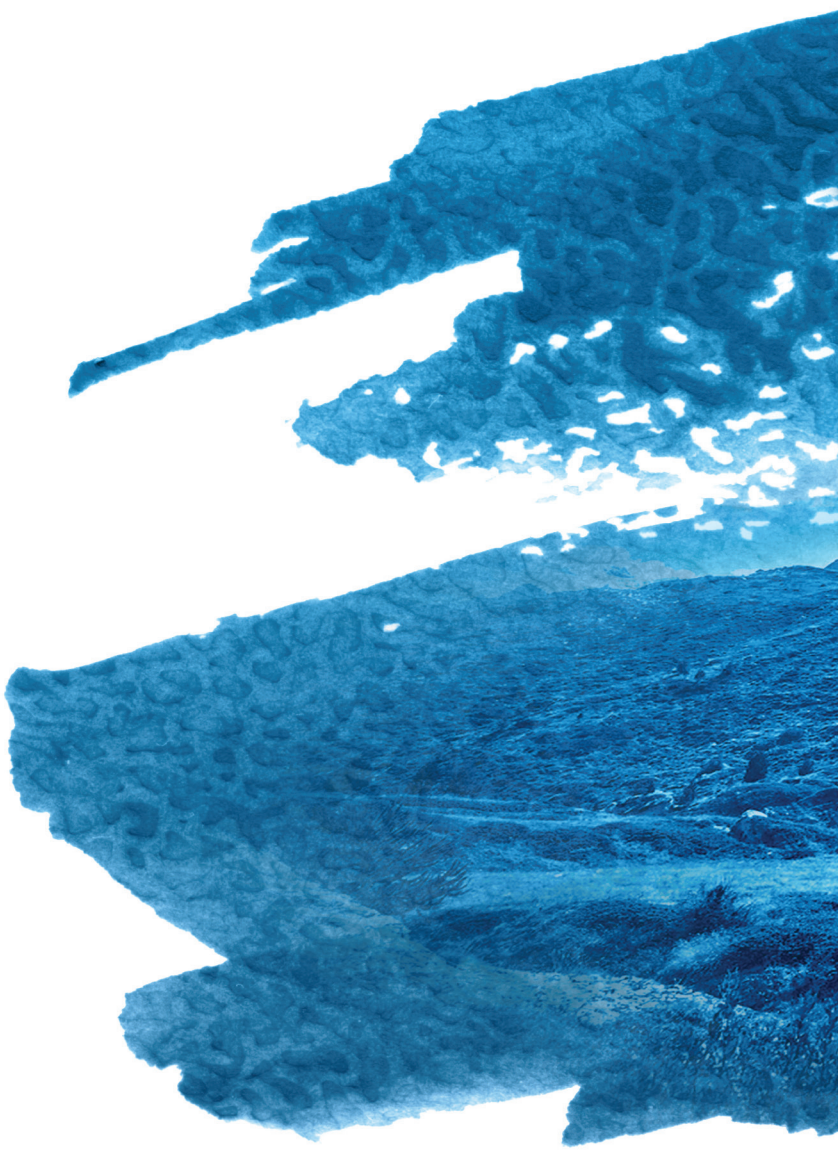
Date: March 12, 2018

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

Date: March 12, 2018

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


Akebia™
THERAPEUTICS



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