Akebia Therapeutics, Inc.
Form 10-K
March 04, 2015

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

x ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2014

OR

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

AKEBIA THERAPEUTICS, INC.

(Exact name of Registrant as specified in its Charter)

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

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

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

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

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

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 x

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 x 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 x NO ¨

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

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

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

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant, based on the closing price of the shares of common stock on The NASDAQ Stock Market on June 30, 2014, was $546,323,693.

The number of shares of Registrant's Common Stock outstanding as of February 28, 2015 was 20,370,624.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the definitive proxy statement for our 2015 Annual Meeting of Stockholders scheduled to be held June 10, 2015 are incorporated by reference into Part III of this annual report on Form 10-K.

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NOTE REGARDING FORWARD-LOOKING STATEMENTS

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

- the projected timing of (1) data from our recently completed Phase 2b study of AKB-6548 in non-dialysis patients with anemia related to chronic kidney disease (CKD), (2) commencement of a Phase 3 development program of AKB-6548, (3) submission of an NDA for AKB-6548 and (4) data from our Phase 2 clinical study of AKB-6548 in CKD patients undergoing dialysis;
- our plans to commercialize AKB-6548, if it is approved;
- our development plans with respect to AKB-6899;
- the timing or likelihood of regulatory filings and approvals, including any required post-marketing testing or any labeling and other restrictions;
- the implementation of our business model and strategic plans for our business, product candidates and technology;
- our competitive position;
- our intellectual property position;
- developments and projections relating to our competitors and our industry;
- our estimates regarding expense, future revenue, capital requirements and needs for additional financing; and
- other risks and uncertainties, including those listed under Part II, Item 1A. Risk Factors.

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

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

NOTE REGARDING STOCK SPLIT

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

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PART I

Item 1. Business

Overview

We are a biopharmaceutical company focused on the development of novel proprietary therapeutics based on hypoxia inducible factor, or HIF, biology and the commercialization of these products for patients with kidney disease. HIF is the primary regulator of the production of red blood cells, or RBCs, in the body and a potentially novel mechanism of treating anemia. We were incorporated in Delaware in 2007.

Our lead product candidate, AKB-6548, is being developed as a once-daily, oral therapy. We have successfully completed a Phase 2b study demonstrating that AKB-6548 can safely and predictably raise hemoglobin levels in non-dialysis patients with anemia related to chronic kidney disease, or CKD.

On October 27, 2014, we announced positive top-line results from our Phase 2b study of AKB-6548 in non-dialysis patients with anemia related to CKD, and we expect complete efficacy and safety data to be presented in the first half of 2015. We expect to initiate Phase 3 studies for anemia secondary to CKD in 2015 and anticipate submitting an NDA for AKB-6548 in the United States by 2019, if the Phase 3 data are favorable. We have also initiated Phase 2 clinical development for AKB-6548 for the treatment of anemia in patients undergoing dialysis, the second indication we will pursue. The results from that study are expected in the third quarter of 2015. We have also commenced discussions with European regulatory authorities in the first quarter of 2015, with the goal of potentially also submitting European marketing application(s). Also in the third quarter of 2014, we completed a thorough QT (TQT) study, demonstrating that AKB-6548 does not have an adverse effect on cardiac repolarization or conduction (i.e., negative TQT study).

Our preclinical candidate, AKB-6899, is a small molecule with minor structural differences from our lead compound AKB-6548. However, AKB-6899 has distinctive biochemical and physiological properties that may be beneficial for treatment of certain cancers. In several preclinical mouse models, AKB-6899 has been active in reducing tumor growth and development of metastases. Therefore, Investigational New Drug, or IND, enabling studies are being performed with the goal of opening an IND with the U.S. Food and Drug Administration (FDA) in 2015.

We own worldwide rights to our HIF-based product candidates, including AKB-6548. If approved by regulatory authorities, we plan to commercialize AKB-6548 in the United States ourselves and intend to seek one or more collaborators to commercialize the product candidate in additional markets.

Anemia is a serious medical condition in which blood is deficient in RBCs and hemoglobin, both of which are critical in delivering oxygen to tissue. Anemia generally exists when hemoglobin, a protein in RBCs that carries oxygen, is less than 13 g/dL in men or 12 g/dL in women. Untreated anemia is associated with chronic fatigue, increased risk of progression of multiple diseases and death. Anemia is common in patients with CKD, cancer, heart failure,

inflammatory diseases and other critical illnesses, as well as in the elderly.

More than 30 million people in the United States have CKD, with estimates that over 1.8 million of these patients suffer from anemia. Anemia from these indications is currently treated by injectable recombinant protein erythropoiesis stimulating agents, or rESAs—including Epogen, Aranesp and Procrit—with iron supplementation or an RBC transfusion. Based on the reported revenues of companies that market and sell rESAs, we estimate that global sales of injectable rESAs were $6.3 billion in 2012, the vast majority of which were for renal indications.

rESAs are designed to stimulate production of RBCs by binding directly to and saturating erythropoietin, or EPO, receptors. While injectable rESAs and transfusions may be effective in raising hemoglobin levels, they carry significant potential side effects and also need to be delivered subcutaneously or intravenously. In particular, injectable rESAs may lead to thrombosis, stroke, myocardial infarction and death, and these risks are described in black box warnings on the prescribing information of all products marketed in this class. These safety concerns, which became evident starting in 2006, have led to a significant reduction in the use of injectable rESAs. Today anemia is either not treated or inadequately treated in the majority of CKD patients, and we believe that a safe, effective, oral therapeutic option will take significant market share and meaningfully grow the market in patients not requiring dialysis.

AKB-6548 works by a differentiated mechanism of action that we believe has the potential to be safer than that of injectable rESAs. This novel mechanism of action is referred to as HIF prolyl-hydroxylase, or HIF-PH, inhibition. Instead of binding directly to the EPO receptors on cells in the bone marrow, AKB-6548 leads to activation of critical pathways for hemoglobin and RBC production. This approach mimics the physiological adjustment made by the body when exposed to reduced oxygen levels at higher altitudes.

To date, AKB-6548 has been studied in ten clinical trials across three separate patient populations: healthy volunteers, patients with CKD stages 3, 4 and 5 (non-dialysis), and patients with end-stage renal disease (ESRD) on hemodialysis. Our Phase 2a trial enrolled 91 patients with anemia secondary to CKD, which showed significantly increased hemoglobin levels among subjects taking AKB-6548 compared to baseline in a dose-dependent manner across all treatment arms ($p < 0.0001$). No drug-related serious adverse events were reported, and dosing was well-tolerated. In addition, AKB-6548 was also shown to stabilize the iron supply to the bone marrow while improving hemoglobin production.

We recently completed a Phase 2b study demonstrating that AKB-6548 can safely and predictably raise hemoglobin levels in non-dialysis patients with anemia secondary to CKD. The results of this Phase 2b study support advancement into Phase 3 to further evaluate the efficacy and safety of AKB-6548 for the treatment of anemia in CKD patients not on dialysis. We plan to initiate Phase 3 global registration studies for AKB-6548 in patients with anemia secondary to CKD in 2015, positioning us to file for approval in the United States by 2019.

Given the burdens of the current standard of care and costs associated with administering an injectable rESA, we believe AKB-6548 is a promising alternative for the overall cost-effective treatment of anemia. We intend to commercialize AKB-6548 ourselves in the United States for the treatment of anemia in patients with CKD. These patients are primarily treated by approximately 7,000 nephrologists, and we believe we can reach most of this market with a specialty sales force of approximately 125 people. We intend to seek one or more commercial collaborators for the development and commercialization of AKB 6548 outside the United States. We may also explore opportunities to expand AKB-6548 into additional markets not adequately addressed by injectable rESAs because of safety or dosing delivery issues.

We are led by a team of experienced biopharmaceutical executives with a background in developing and commercializing drugs for the treatment of renal and metabolic disorders. John P. Butler, our CEO, was former President of Genzyme Corporation’s renal division which grew to over $1 billion in annual revenue under his leadership, and is currently the Chairman of the Board of the American Kidney Fund, the leading patient advocacy organization for kidney disease patients. Earlier in his career, Mr. Butler held sales and marketing positions at Amgen, working on the early commercial launch of injectable rESAs in the renal anemia market.

Our Strategy

Our strategy is to develop novel therapeutics for patients based on HIF biology and to commercialize products for patients with kidney disease, beginning with AKB-6548 for patients with anemia secondary to CKD. The key elements of our strategy are to:

- Complete the development of AKB-6548 for anemia secondary to CKD. We intend to initiate a Phase 3 development program in 2015 following our end of Phase 2 meeting with the United States Food and Drug Administration, or FDA.

- Obtain regulatory approval of AKB-6548 for anemia secondary to CKD in the United States, Europe and other markets. We plan to complete an end of Phase 2 meeting with the FDA and seek scientific advice from the European Medicines Agency, or EMA, to define the Phase 3 development program necessary to secure regulatory approval to market AKB-6548. We would expect to initiate Phase 3 trials for anemia secondary to CKD in 2015, and anticipate submitting an NDA for AKB-6548 in the United States by 2019 if the Phase 3 data are favorable.

- Commercialize AKB-6548 in the United States and other territories. We will establish a specialty sales and marketing organization to commercialize AKB-6548 in the United States. Outside of the United States, we intend to seek one or more commercial collaborators.

- Advance AKB-6899 into clinical development. We plan to advance AKB-6899, a second HIF-PH inhibitor product candidate, which we believe, based on preclinical testing, has the ability to increase EPO levels while reducing vascular endothelial growth factor, or VEGF, levels. We intend to file an Investigational New Drug, or IND, application and begin a Phase 1 trial to determine its potential use in oncology.

- Acquire or in-license additional nephrology products. We will look to diversity our pipeline with additional products that would be prescribed by nephrologists.

We may enter into strategic collaborations to fully realize elements of our strategy.

Our Product Candidates

The following chart depicts our HIF-based product candidates, their indications and their current development.

Anemia Overview

Anemia is a serious medical condition in which blood is deficient in RBCs and hemoglobin, leading to inadequate oxygen delivery to tissues and cells throughout the body. RBCs are normally formed in the bone marrow from precursor or progenitor cells. EPO, a hormonal factor primarily produced in the kidney and liver, binds to and activates the EPO receptor on these precursor cells. The activation of the EPO receptor stimulates these cells to divide, differentiate into RBCs that contain hemoglobin, and mobilize into circulation. Hemoglobin is an iron-containing protein in RBCs that transports oxygen to, and carbon dioxide from, the tissues of the body.

Anemia generally exists when hemoglobin is less than 13 g/dL in men and 12 g/dL in women. Anemia has a number of potential causes, including nutritional deficiencies, iron deficiency, bone marrow disease, medications, and abnormalities in EPO production or sensitivity. Common causes of anemia due to inadequate EPO production include CKD, age, heart failure, inflammatory diseases, cancer and other critical illnesses.

Untreated anemia is associated with chronic fatigue, increased risk of progression of multiple diseases, and death. This morbidity and mortality risk has been clearly shown in the CKD population, where in patients age 66 and older, anemic patients with mid-stage CKD (Stage 3) have a 149% increase in cardiovascular events and patients with severe CKD (Stage 4 and 5) have a 24% increase in cardiovascular events versus non-anemic patients in the same group, according to a paper published in 2006 in the peer-reviewed journal Blood. Similarly, compared to non-anemic patients, anemia increases the mortality rate by 199% in mid-stage CKD, and 59% in severe CKD. Successful treatment of anemia significantly improves patients' quality of life, especially with respect to vitality, fatigue and physical function. In addition, patients whose anemia has been successfully treated have demonstrated lower mortality rates, less frequent hospitalization, and decreases in cardiovascular morbidity.

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 can cause waste products to build up in the patient's blood and can lead to other health problems, including cardiovascular disease, anemia, and bone disease. CKD patients are classified by the degree of their loss of kidney function as measured by the glomerular filtration rate, or GFR, and albuminuria, the protein levels in urine. As seen in the table below, CKD affects more than 30 million people in the United States and the prevalence of anemia increases with the severity of CKD.

There are many causes of CKD, the most common of which are diabetes mellitus and hypertension. The prevalence and incidence of CKD is increasing in all segments of the U.S. population, particularly in patients over 65, as shown below. Risk factors for the development of CKD include underlying disease (hypertension, diabetes and cardiovascular disease), lifestyle factors (tobacco use and inactivity), family history, aging, and prenatal factors (maternal diabetes mellitus, low birth weight and small-for-gestational-age status). According to a Lancet article from May 2013, projected worldwide population changes suggest that the potential number of cases of kidney disease, specifically end-stage, will increase disproportionately in developing countries, such as China and India, where the numbers of elderly people are expanding. This effect will be enhanced further if the trends of increasing hypertension and diabetes prevalence persist, competing causes of death—such as stroke and cardiovascular diseases—are reduced, and access to treatment improves.

The prevalence and severity of anemia in CKD increases as renal function deteriorates. Three variables which may combine to accentuate and accelerate anemia as CKD progresses include:

- Peritubular fibroblasts, a type of cell in the kidney, are designed to sense the amount of oxygen carried by the blood. These cells secrete EPO to adjust the production of RBCs and maintain circulating oxygen levels at normal physiologic levels. As kidney disease progresses, the number of peritubular fibroblasts is reduced and EPO secretion is significantly decreased. This decline in EPO leads to a reduction in RBC production.

- CKD leads to a shorter average life span for RBCs (70 days) as compared to healthy individuals (90 to 120 days), requiring increased RBC production to keep RBC levels consistent with those of a healthy individual.

- The availability of iron to the bone marrow is impaired. Iron is a required component in the formation of hemoglobin, and is essential in the transport of oxygen.

As CKD progresses, the combined effect of decreased RBC production from lower EPO signaling, increased rate of RBC destruction, and reduced iron availability to the bone marrow results in the increased prevalence and severity of anemia.

Current Treatments Leave a Substantial Unmet Need

Injectable rESAs, including epoetin alfa, epoetin beta, and darbepoetin alfa, are currently the standard of care for treating anemia in patients with CKD and must be administered intravenously or subcutaneously along with iron supplements. Based on the reported revenues of companies that market and sell rESAs, we estimate that global sales of injectable rESAs were $6.3 billion in 2012, as compared to an estimated $12 billion in 2006. Of these 2012

revenues, an estimated $3.4 billion were generated in the United States, the vast majority of which were for renal indications. In 2006, data on the risks of rESA use among these patients started to become available, forcing physicians to balance serious safety concerns against the efficacy of rESAs. The safety concerns with injectable rESA use include increased risk of cardiovascular disease as well as a potentially increased rate of tumor progression in patients with cancer. We believe that the decline in market revenue since 2007 is a direct result of these increased safety concerns, as well as

reimbursement pressures, and that an opportunity exists for a safer, well-tolerated alternative to replace injectable rESAs as the standard of care for anemia secondary to CKD.

As a result of the safety concerns related to rESA use, patients have been forced to live with lower hemoglobin levels, higher rates of transfusions, and more intravenous iron, or IV iron, use. The percentage of dialysis patients in the United States receiving IV iron has increased from 50% in 1999 to 71% during in 2011. Among U.S. patients receiving IV iron, the mean monthly dose has also increased by 21%. Despite the increased use of IV iron and the rate of RBC transfusions, patients are still subject to safety risks related to these alternative treatments to injectable rESAs. The risks of RBC transfusions include the development of antibodies to foreign antigens, transmission of blood-borne pathogens, impairment of venous access in CKD patients (not on dialysis) and iron overload with chronic transfusions. The risks of IV iron include hypersensitivity reactions, such as fatal anaphylactic-type reactions.

Currently, there is no scientific consensus regarding the cause of the adverse cardiovascular outcomes associated with the use of injectable rESAs to normalize hemoglobin levels. The results of the four major randomized, controlled clinical trials on the treatment of anemia secondary to CKD with rESAs and adjunctive iron supplementation (Normal Hematocrit Trial/NHCT, CREATE, CHOIR and TREAT) all showed an increased risk of adverse cardiovascular outcomes. These results were surprising at the time and contradicted the extensive body of data from observational studies that showed reduced mortality and improved health outcomes to be associated with higher hemoglobin levels.

A number of critical post-hoc analyses of the data from randomized controlled clinical trials have shifted attention to the potential of dose-related toxicity of injectable rESAs in CKD patients as a contributing factor to the reported adverse cardiovascular outcomes, instead of the role of normalized hemoglobin levels. The strongest correlation of adverse outcomes in the post-hoc analyses has been to the level of the injectable rESA dose, not the hemoglobin level achieved. All of the studies analyzed to date demonstrate that both non-dialysis and dialysis-dependent CKD subjects who achieved normal hemoglobin levels had better clinical outcomes than subjects assigned to higher hemoglobin targets who failed to reach the assigned level despite increasing doses of injectable rESAs. In addition, CKD patients who were able to achieve and maintain normal hemoglobin levels through means other than the use of injectable rESAs (such as hypoxia or iron supplementation) experienced fewer cardiovascular events and reduced morbidity and mortality. Recent studies of injectable rESA use in various preclinical models (including non-human primates) also showed that the frequency of mortality and thrombotic events cannot be explained solely by the achieved higher hemoglobin levels, rather, they are related to the dose, dose frequency, and dose duration of injectable rESAs.

The graphs below highlight these findings. The first chart explores the relative risk of serious cardiovascular adverse events, including death, hospitalization for heart failure, stroke or myocardial infarction based upon the hemoglobin achieved during the study as well as the weekly injectable rESA dose. The data clearly show that the risk of adverse cardiovascular events was greatest in those patients receiving the highest injectable rESA doses, regardless of the hemoglobin level that was achieved.

The second graph explores the probability of reaching one of several adverse events (death, stroke, heart failure or myocardial infarction) over time for two different groups:

- patients who achieve the target hemoglobin level with a low injectable rESA dose, and
- patients who do not reach the target hemoglobin level, but receive a high injectable rESA dose in an effort to reach the target level.

This chart is consistent with the previous chart as it shows that patients with high hemoglobin levels on low injectable rESA doses have better outcomes than patients with high injectable rESA doses and low hemoglobin levels. Therefore, high injectable rESA doses, not high hemoglobin levels, appear to be correlated most strongly with adverse outcomes.

The significant safety risks associated with rESAs are outlined in a black-box warning in their prescribing information. This warning arose from numerous events highlighting the safety concerns of injectable rESAs and the responses by the FDA, as highlighted below.

- In 2007, as a result of concerns associated with administering injectable rESAs to target higher hemoglobin levels, the FDA required that revised warnings, including black-box warnings, be added to the labels of marketed injectable rESAs advising physicians to monitor hemoglobin levels and use the lowest dose of injectable rESA, and increase the hemoglobin concentration to the lowest level sufficient to avoid the need for RBC transfusions.
- In November 2007, the FDA found evidence that the use of injectable rESAs to increase hemoglobin to more than 12 g/dL can stimulate progression of some cancers. As a result, injectable rESAs were required to contain black-box labeling for this risk. Following this change in labeling, the use of injectable rESAs in cancer patients has declined significantly.

- In late 2009, Amgen announced the results from the Trial to Reduce Cardiovascular Endpoints with Aranesp Therapy, or TREAT, its large, randomized, double-blind, placebo-controlled Phase 3 study of patients with CKD (not requiring dialysis), anemia and type 2 diabetes. In this study, Aranesp was used to treat anemia to a target hemoglobin level of 13 g/dL, which was higher than the 10 g/dL - 12 g/dL range previously approved by the FDA in the label. Study results failed to show a benefit compared to the control group with regard to composite of time to all-cause mortality or cardiovascular morbidity (including heart failure, heart attack, stroke, or hospitalization for myocardial ischemia) and composite of time to all-cause mortality or chronic renal replacement therapy. In addition, higher rates of stroke were reported among patients in the 13 g/dL target group compared to the control group. Finally, among a subgroup of patients with a history of cancer at baseline, a statistically significant increase in deaths from cancer was observed in the Aranesp-treated patients compared to placebo-treated patients.

- In January 2010, FDA officials published an editorial in the New England Journal of Medicine noting that a number of randomized trials, including TREAT, had attempted to show that using injectable rESAs to raise hemoglobin concentrations to higher targets improves clinical outcomes but instead suggested the opposite. Accordingly, the article indicated that more conservative hemoglobin targets (well below 12 g/dL), more frequent hemoglobin monitoring, and more cautious dosing should be evaluated.

- In February 2010, the FDA required that injectable rESAs be prescribed and used under a REMS to ensure the safe use of the drugs. As part of the REMS, a medication guide explaining the risks and benefits of injectable rESAs must be provided to all patients receiving injectable rESAs for all indications, and the FDA imposed reporting and monitoring obligations on the manufacturers to ensure compliance.

- In June 2011, the FDA cited increased risks of cardiovascular events as a basis for more conservative dosing guidelines for use of injectable rESAs in CKD patients and announced related changes to injectable rESA labeling. The FDA removed the prior target hemoglobin range of 10-12 g/dL, and recommended that CKD patients initiate treatment when the hemoglobin level is less than 10 g/dL and reduce or interrupt dosing if the hemoglobin level approaches or exceeds 10 g/dL for non-dialysis patients and 11 g/dL for dialysis patients. The FDA also required Amgen to conduct additional clinical trials to explore dosing strategies to minimize hemoglobin variability, rates of change and excursions.

We believe there is now substantial evidence to suggest that EPO level, not hemoglobin, is the cause of the safety issues in the above trials. The collective preclinical and clinical data support a critical re-thinking on the best approach to treating anemia, the appropriate and safe hemoglobin target, and the right time to initiate treatment for these patients.

AKB-6548 as a potential solution

We are developing our lead product candidate, AKB-6548, to be a best-in-class HIF-PH inhibitor for the treatment of anemia secondary to CKD. AKB-6548 may potentially offer:

- Predictable, meaningful and sustained improvements in hemoglobin levels;

- Once-a-day therapy delivered orally;

- A dosing regimen that restores the normal diurnal EPO pattern;

- Robust pharmacodynamics and substantially lower peak EPO levels than with injectable rESAs; and

- Reduced administration of IV or oral iron supplementation to patients treated for anemia secondary to CKD.

Novel Mechanism of Action, Which Mimics the Body's Natural Physiologic Response

AKB-6548 is designed to work by a mechanism of action that differs from injectable rESAs. This novel mechanism of action is referred to as a HIF-PH inhibitor. Instead of binding directly to and saturating the EPO receptors in the bone marrow for prolonged periods of time, HIF-PH inhibitors act by simulating the body's natural response to anemia. In this way, AKB-6548 achieves a controlled, adaptive stimulation of the erythropoietic system in the body. This activation of the whole system results in both increased RBC production and improved stabilization of the bone marrow's iron supply, which ensures the proper incorporation of iron into hemoglobin necessary for RBC production. This adaptive simulation is very similar to the natural response that is induced when a person ascends in altitude. At higher altitudes, low levels of oxygen circulating in the blood stream lead to reduced HIF-PH activity in relevant cells in the kidney and liver. The reduced HIF-PH activity stabilizes and increases levels of HIFa proteins (HIF1a and HIF2a) in these cells. For most cells, the stabilization of HIF2a is greater than that of HIF1a, ultimately leading to an increase in EPO secretion and a subsequent increase in RBC production.

HIF-PH inhibitors work by blocking the effect of the prolyl-hydroxylase enzymes, which promote the breakdown of HIFa proteins. As the breakdown is inhibited, the level of these HIFa proteins increases in cells. These HIFs are the primary protein mediators that enable the body and all of its individual cells to adapt to changes in levels of oxygen. Both HIF1a and HIF2a proteins are consistently produced and their levels in cells are adjusted by the activity of the HIF-PH enzymes, which target the HIFa proteins for degradation. HIF1a helps cells survive under very low oxygen conditions, whereas HIF2a helps cells and the body to adapt to modest changes in oxygen, such that would occur with a change in altitude from sea level to up to 7,500 feet.

When HIFa is stabilized, it travels to the nucleus of the cell, where it binds to the protein HIFß. When bound together, they induce the genetic signal for the production of EPO and several other proteins. The HIF-PH inhibitors increase HIFa levels in much the same way that a reduction in oxygen increases HIFa levels by inhibiting the HIF-PH enzymes in the body. With continued stabilization of HIFa (either by staying at higher altitude or by daily dosing of the HIF-PH inhibitor), the level of hemoglobin and RBCs will rise in order to increase the amount of oxygen circulating in the blood. In this way, once-daily dosing of AKB-6548 may have the potential to restore the normal level of EPO for a patient with anemia.

AKB-6548, our lead compound in development, works by inhibiting HIF-PH, leading to stabilization and increased levels of HIFa, and improved production of hemoglobin and RBCs, while maintaining normal levels of EPO in patients. In addition, we believe that AKB-6548's mechanism of action provides for the ability to induce a more prominent HIF2a response (as naturally occurs with a moderate increase in altitude), and an enhancement in the normal diurnal variation of EPO, which is the normal rise and fall of EPO during the each day.

This mechanism of action is illustrated in the graphic below.

Potential Best-in-Class Profile

We believe AKB-6548 has compelling clinical data demonstrating a best-in-class profile with several potential safety and efficacy advantages over current injectable rESA therapy for the treatment of anemia secondary to CKD.

- AKB-6548 significantly increases hemoglobin in anemic CKD patients. We have successfully completed two Phase 2 trials, in which AKB-6548 significantly increased hemoglobin levels. In the first study (CI-0005), AKB-6548 was demonstrated to raise hemoglobin in a dose-dependent manner compared to baseline and across all treatment arms ($p < 0.0001$). In the second Phase 2 study (CI-0007), AKB-6548 effectively increased hemoglobin while the dose was adjusted in accordance with a dosing algorithm ($p = 0.0001$ compared to placebo). The purpose of the algorithm was

to minimize the frequency of increases in hemoglobin ³ 13.0 g/dL. Only 4.3% of subjects on AKB-6548 had single excursions ³ 13.0 g/dL. Further, AKB-6548 provides a physiologic reticulocyte, or newly formed RBC, response, which leads to a more gradual and consistent increase in hemoglobin levels than what is

seen with injectable rESA therapies, reducing the likelihood of a patient's hemoglobin to rising to levels that cause concern.

- AKB-6548 may have the potential to restore the normal diurnal variation of EPO for a patient with anemia in a way that an injectable rESA cannot. Instead of binding directly to and saturating the EPO receptor for prolonged periods of time as is the case with current injectable rESA treatments, AKB-6548 acts by simulating the body's natural response to hypoxia that is carried out by stabilization of HIFa. We believe the manner in which AKB-6548 works permits a more prominent HIF2a response (as naturally occurs with a moderate increase in altitude) and there is an enhancement in the normal diurnal variation in EPO, which is the normal rise and fall of EPO during the each day, without continuous elevation of EPO levels. The graph below illustrates the EPO levels that are obtained with AKB-6548 compared with doses of Aranesp and Epogen.

- Oral, once-daily dosing. Once daily, oral dosing of AKB-6548 offers improved convenience for patients as compared to injectable rESAs. This convenience may increase access to anemia therapy for the largely underserved population of patients with anemia secondary to CKD who are not yet on dialysis and for patients with other forms of anemia. AKB-6548 offers the potential of flexible oral dosing that provides a more gradual and reliable means of titration than that of injectable rESAs.

- Ability to stabilize the iron supply to the bone marrow while improving hemoglobin production. In clinical trials, AKB-6548 has demonstrated dose-related increases in iron mobilization and total iron binding capacity. These results indicate that AKB-6548 will stabilize the iron supply to the bone marrow while improving hemoglobin production and should improve EPO responsiveness. As a result, unlike injectable rESAs which have no effect on iron mobilization, AKB-6548 offers the added potential benefit of reducing the amount of supplemental iron required by anemia patients.

- Differentiated safety profile. AKB-6548's novel mechanism of action and dosing profile offer the opportunity to potentially avoid the black box label ascribed to injectable rESAs. In our recently completed Phase 2b study, AKBA-6548 was generally well tolerated with no safety concern identified.

AKB-6548 Clinical Development Overview

Early Clinical Studies (CI-0001 to CI-0004, and CI-0006):

An IND was filed for AKB-6548 for the treatment of anemia associated with CKD and chronic renal failure on July 17, 2009. Under the IND, we may investigate AKB-6548 in subjects who are not on dialysis and in subjects who are on dialysis. To date, AKB-6548 has been studied in ten clinical trials across three separate patient populations: healthy volunteers, patients with CKD stages 3, 4, and 5 (non-dialysis), and patients with end-stage renal disease (ESRD) on hemodialysis. These clinical trials consisted of one Phase 2b clinical trial, four Phase 2a clinical trials and five Phase 1 clinical trials. The early clinical studies (CI-0001 through CI-0004) for AKB-6548 were designed to demonstrate the efficacy and safety of the compound, starting in healthy male volunteers and progressing to CKD patients with anemia. In healthy males, we demonstrated that AKB-6548 can be dosed daily, and that it induces the desired pharmacodynamics effect, specifically:

- the induction of enhanced diurnal EPO secretion from a single dose;

- an increase in new RBC production by day 5 of dosing; and

- an increase in hemoglobin levels by day 10 of dosing.

Subsequently, we demonstrated a similar induction of a diurnal EPO response in CKD patients. This was followed by a 28 day, dose-titration study to establish the necessary dosing information for increasing hemoglobin levels. Throughout these studies, AKB-6548 was generally well tolerated. There were no serious adverse events, or SAEs, and treatment emergent adverse events, or TEAEs, were limited in number and duration.

The most common potentially drug-related adverse events, or AEs, in our eight clinical trials were gastro-intestinal disorders, including diarrhea, nausea and constipation. In our CI-0001 trial, there was one subject who had diarrhea that was considered potentially related to the study drug. In our CI-0002 trial, the potentially drug-related TEAEs were gastroesophageal reflux and dyspepsia, each reported in separate subjects. In our CI-0006 trial, three of the eight subjects in the capsule group reported potentially drug-related AEs (nausea in two subjects and headache and dizziness in one subject each), and one of the eight subjects in the tablet group reported potentially drug-related headache and dizziness. In our CI-0003 trial, five subjects experienced AEs that were considered potentially drug-related. Two subjects had nausea. Other potentially drug-related AEs that were noted once included tachycardia, vomiting, pyrexia, upper respiratory tract infection, hypomagnesemia, myalgia, headache, somnolence, tremor, oropharyngeal pain, cold sweat and hypotension. In our CI-0004 trial, three subjects had potentially drug-related TEAEs, including nausea, chills, peripheral neuropathy, peripheral sensory neuropathy and muscle spasms. In our CI-0005 trial, the most frequently reported TEAEs considered to be potentially drug-related were gastrointestinal disorders, including one subject with abdominal discomfort, three subjects with constipation, one subject with diarrhea

and two subjects with nausea. Other one-time events in the CI-0005 trial that were considered to be potentially drug-related included neutropenia, cardiac palpitations, decreased transferrin saturation, muscle spasms, dizziness, pollakiuria, hypertension and abnormal hair texture.

The individual design and summary results of each of our completed clinical trials are highlighted below:

Study	Study Design Subject	Design (Endpoint)	Dose, Duration [1]	Subjects Treated AKB-6548	Placebo	Key Findings
Phase 1						
CI-0001	Healthy males	Double-blind, placebo-controlled, fasted (Safety/PK/PD)	80 mg, 160 mg, 300 mg, 600 mg, 900 mg, 1200 mg; single dose	6 (80 mg) 6 (160 mg) 6 (300 mg) 6 (600 mg) 6 (900 mg) 6 (1200 mg)	12 (2 per cohort)	AKB 6548 was well tolerated, and dose responsive increases in EPO levels were demonstrated following a single dose. Half-life of the compound was measured at approximately 4.8 hours. Ten subjects had an adverse event (AE) (seven in the AKB 6548 group and three in the placebo group). No serious adverse events (SAEs) were reported.
CI-0002	Healthy males	Double-blind, placebo-controlled, fasted (Safety/PK/PD)	500 mg, 700 mg, 900 mg; 10 days	8 (500 mg) 9 (700 mg) 8 (900 mg)	9 (3 per cohort)	AKB 6548 was well tolerated, and dose responsive increases in reticulocytes and hemoglobin levels were demonstrated. It was also shown that EPO levels returned to baseline by 24 hours following each dose. 26 subjects reported a treatment-emergent adverse event (TEAE). These were evenly distributed across dosing groups. No SAEs were reported.
CI-0006	Healthy males	Randomized, cross-over bioavailability study, fasted (Bioavailability /PK)	315 mg; single dose of capsule and tablet, with three days wash-out period between doses	8	0	Both capsules and tablets were well tolerated following a single dose, and shown to be bioequivalent. Six subjects had AEs considered related to study drug. No SAEs were reported.
CI-0008	Healthy volunteers	Mass Balance (Radioactivity/ PK)	650 mg; single dose (100 mCi ^{14}C-AKB-6548)	6	0	The drug was generally well tolerated during this study. There were no SAEs and no subjects dropped out of the study. Total radioactivity recovery in urine and feces was >85% with approximately 60% in urine and approximately 26% in feces. Majority of the drug-related radioactivity (>75%) in plasma was associated with AKB 6548, followed by the AKB 6548-O-Glucuronide (~15%) and a very low contribution (<1%) coming

from the AKB 6548-Acyl-Glucuronide.

Study Design				Subjects Treated		
Study	Subject	Design (Endpoint)	Dose, Duration [1]	AKB-6548	Placebo	Key Findings
CI-0009	End-stage renal disease (ESRD)	Randomized, crossover, pharmacokinetic study with 72 hour wash-out between successive dosing (PK/Safety and tolerability of subjects on chronic hemodialysis)	450 mg dose four hours prior to start of a hemodialysis session; 450 mg dose 2 hours after completion of a different dialysis session	12	0	During the study, dosing of the drug was well tolerated. No SAEs were reported during dosing and over the 48-hr in-house observation period after each of the pre-dialysis and post-dialysis dose administrations, although one subject experienced an exacerbation of a concurrent diabetic foot ulcer resulting in 2 reported SAEs during the follow-up period, 7 days after the last sample collection. These 2 events were considered unrelated to the study drug. The timing of administration of AKB-6548 doses (pre- or post-hemodialysis) did not markedly affect pharmacokinetics of AKB 6548 and two measured glucuronide metabolites. The hemodialysis procedure had minimal impact on the clearance of AKB 6548.
CI-0010	Healthy volunteers	Randomized, partially double-blind, single-dose, 4 treatment, 4 period, 4 sequence crossover study to evaluate the effect of AKB 6548 on cardiac repolarization intervals (Thorough QTc Study)	600 mg AKB-6548 tablet; 1200 mg AKB-6548 tablet; placebo tablets, 400 mg moxifloxacin tablet	49	48	In general, study drug was well tolerated with no SAEs reported. AKB 6548 did not have a meaningful effect on any ECG parameters. An effect on the QTcF interval exceeding 10 msec could be confidently excluded and the effects on heart rate, PR interval, and QRS interval were small and clinically not relevant.
Phase 2						
CI-0003	CKD, Stages 3 & 4	Open-label, fed (Safety/PK/PD)	500 mg; single dose	22	0	Following a single dose of 500 mg of AKB 6548, the changes in EPO levels followed a similar pattern as that observed in the Phase 1 study at 600 mg in healthy volunteers (CI-0001). In these subjects with CKD, peak levels of EPO were similar to healthy male volunteers, and the half-life was modestly longer at 7.9 hours. Dosing was well

tolerated. Five subjects had AEs considered related to study drug. No SAEs were reported.

Study	Study Design Subject	Design (Endpoint)	Dose, Duration [1]	Subjects Treated AKB-6548	Placebo	Key Findings
CI-0004	CKD, Stages 3 & 4	Open-label (Safety/Change in Hgb, hematocrit, reticulocytes)	Within subject, dose escalation (potential doses of 200 mg, 300 mg, 400 mg, 500 mg, 600 mg, and 700 mg); 28 days of dosing	10	0	In this study, subjects started at 300 mg (CKD 4) or 400 mg (CKD 3). Dose adjustments could be made weekly based on reticulocyte count and hemoglobin data. Dosing was well tolerated. Average hemoglobin levels rose from 9.91 g/dL at baseline to 10.54 g/dL by Day 29. Three subjects had AEs considered related to study drug. No SAEs were reported.
CI-0005	CKD, Stages 3, 4 & 5, not on dialysis	Double-blind, placebo-controlled (Mean absolute change in Hgb between the pre-dose average and End of Treatment/ PD/PK)	240 mg, 370 mg, 500 mg, 630 mg; 42 days of dosing	18 (240 mg) 18 (370 mg) 17 (500 mg) 19 (630 mg)	19	Dosing was well tolerated. AKB 6548 significantly increased hemoglobin levels in subjects compared to baseline in all dose groups and compared to placebo. The hemoglobin increase occurred without increasing pre-dose EPO levels (prior to daily AKB-6548 dose). Ten subjects had AEs considered related to study drug. There were eight reported SAEs in separated subjects which were all considered unrelated to study drug.
CI-0007	CKD, Stages 3, 4 & 5, not on dialysis (naïve to ESA, previously treated with ESA, or actively treated with ESA)	Double-blind, placebo-controlled (Achieving or maintaining a mean Hgb of ≥ 11.0 g/dL or increasing Hgb by ≥ 1.2 g/dL)	450 mg starting dose with dose adjustment with allowable dose levels of 150, 300, 450, or 600 mg to maintain Hgb <13.0 g/dL; 2:1 active:placebo; 20 weeks of dosing	138	72	The study achieved its primary endpoint and AKB 6548 was generally well tolerated, confirming that the once-daily, oral therapy can successfully increase and maintain hemoglobin (Hgb) levels. 54.9% of patients who received AKB 6548 met the primary endpoint versus 10.3% in the placebo group (p<0.0001; achieving or maintaining a mean Hgb ≥ 11.0 g/dL or increasing Hgb by ≥ 1.2 g/dL above the pre-treatment value as measured by the mean Hgb value at weeks 19 and 20). TEAEs with AKB 6548 were consistent with those reported in

past studies and were well balanced overall between the active and placebo treatment groups (74.6% and 73.6%, respectively). There was a higher incidence of SAEs reported in the active treatment group versus the placebo group (23.9% and 15.3%, respectively), the most common being renal-related. Of the 49 SAEs reported in the active treatment group, one was considered probably related to active treatment and two were considered possibly related, including one death. There were two additional deaths in the treatment group, neither of which was considered drug-related.

[1] All doses were administered orally, once-daily.

CI-0005: Positive Phase 2a Proof of Concept Trial

CI-0005 was designed to confirm the findings of the early clinical studies and to demonstrate efficacy in CKD patients. In November 2012, we presented at the American Society of Nephrology the results of a randomized, double-blind, placebo controlled trial of AKB-6548 in patients with CKD stages 3, 4 and 5 (not on dialysis) to evaluate the change in hemoglobin levels over 42 days at multiple dose levels. The study enrolled 93 patients with CKD stages 3, 4, or 5 (not on dialysis) who initiated treatment with either placebo or AKB-6548 in the following dose groups: 240 mg, 370 mg, 500 mg, or 630 mg once-daily for 42 days. Depending upon hemoglobin response, patients may have had their initial dose titrated to avoid too rapid of a rise in hemoglobin levels.

The primary endpoint for the trial was the mean absolute change in hemoglobin from baseline. As shown in the first graphic below, the study results show all doses of AKB-6548 increased hemoglobin significantly compared with placebo. A one-way analysis of variance, or ANOVA, test showed a statistically significant increase in mean absolute hemoglobin from baseline to week 6 for treatment compared with placebo ($p<0.0001$). The 95% simultaneous confidence limits for the four AKB-6548 treatment groups all showed significant increases in mean absolute hemoglobin from baseline to week 6.

At Day 42, AKB-6548 significantly increased hemoglobin levels in a dose-dependent manner compared to baseline in all dose groups. Important findings included:

1. AKB-6548 treated patients experienced a statistically significant mean increase in hemoglobin, ranging from 0.7 to 1.4 g/dL by Day 42, while placebo-treated patients experienced a small mean decrease in hemoglobin of 0.1 g/dL. The average baseline hemoglobin level was 9.8 g/dL.

2. No patient's measured hemoglobin level exceeded 13 g/dL throughout the study period.

3. The dose-dependent increases in hemoglobin occurred even though 26% of patients in the 630 mg dose and 11% of patients in the 500 mg dose decreased their dose, per protocol, as a result of a hemoglobin increase of greater than 1.5 g/dL or more by Day 28.

4. The increase in hemoglobin levels occurred without increasing pre-dose EPO levels (prior to daily AKB-6548 dose), demonstrating that AKB-6548 is able to improve RBC production without chronically elevating the body's EPO levels.

5. The increase in hemoglobin levels was preceded by an increase in reticulocytes showing that an increase in hemoglobin levels is a result of a physiologic increase in RBC production.

6. A dose-related increase in TIBC indicated enhanced ability to stabilize the iron supply to the bone marrow while improving hemoglobin production, as shown below with the dose-dependent increase in TIBC.

AKB-6548 was generally well tolerated in the 91 subjects who received study drug. In total, 45 subjects had an AE: 34 (47.2%) in the AKB-6548 groups and 11 (57.9%) in the placebo group. AEs were evenly distributed across the dosing groups with no apparent dose related effect. Ten subjects (13.9%) treated with AKB-6548 and one placebo subject (5.3%) had AEs that were considered study drug related.

There were eight SAEs in separate subjects which were all considered unrelated to the study drug by the study investigators; seven in the AKB-6548 groups (9.7%) and one in the placebo group (5.3%). These included fluid overload (placebo patient), gastroenteritis, hypoglycemic event, dizziness, triple vessel coronary artery disease with non-ST elevation myocardial infarction, hypertensive crisis, ventricular pacemaker lead replacement, and azotemia (uremia). One subject, who we believe received only three or four doses of study drug, died after being hospitalized for uremia. The subject’s death occurred several days into her hospitalization following an in-hospital procedure when she developed sustained ventricular tachycardia and cardiac arrest. The subject’s death was not considered to be related to AKB-6548. All other subjects recovered.

VEGF is necessary for the maintenance of healthy kidney function and is regulated by HIF1a. Clinical studies have shown that increased VEGF levels are potentially linked to increased growth of tumors in patients with cancer. AKB-6548 provides for the ability to induce a more prominent HIF2a response, and consistent with this mechanism, no statistically significant change in VEGF levels were observed from baseline for any of the AKB-6548 dose groups.

We also found no statistically significant change in inflammation (C-reactive protein), renal function (Cystatin-C), heart rate, blood pressure and EKG values (including QT assessments).

Phase 2b Study (CI-0007)

We have completed a Phase 2b study of AKB-6548 in subjects with anemia (hemoglobin £ 10.5 g/dL) secondary to CKD not requiring dialysis. This double-blind, randomized, placebo controlled study evaluated the efficacy and safety of AKB-6548 in 210 subjects across 62 U.S. sites. The study enrolled patients based on their prior treatment with rESAs: naïve (never received rESA therapy), previously treated with rESAs, and actively treated with rESAs (previous history of hemoglobin £ 10.5 g/dL). Patients initiated treatment with either 450mg of AKB-6548 or placebo once-daily for 20 weeks. The dose of AKB-6548 was adjusted in accordance with the patient's hemoglobin response. The primary purpose of this study was to demonstrate an adaptive approach to dosing AKB-6548 that would enable subjects to appropriately raise their hemoglobin from baseline without excessive excursions to ³ 13.0 g/dL. Subjects were extensively evaluated for clinical and laboratory safety, changes in specific biomarkers, and changes in quality of life and neuro-cognitive outcomes.

Patients were assigned in a double-blind fashion in a 2:1 ratio to either AKB-6548 or placebo. After initiating treatment at 450 mg, the dose was adjusted in accordance with the protocol defined "Dose Adjustment Guidelines and Algorithm."

The primary endpoint (determined from values at Weeks 19 and 20) of this study was the percent of subjects who either (i) achieve a mean hemoglobin of ³ 11.0 g/dL, or (ii) increase their hemoglobin by ³ 1.2 g/dL over their pre-dose average hemoglobin between screening and baseline. Subjects who received injectable rESA or transfusion rescue were counted as treatment failures and subjects receiving transfusion for a non-rescue reason were removed from the primary analysis. Treatment with AKB-6548 was very effective, compared to placebo, in achieving the primary endpoint ($p<0.0001$).

The results from this study will enable Akebia to determine the optimal dosage, including tablet size and number of tablets per dose, and dose adjustment for the Phase 3 studies. Preliminary analysis indicates that the range of doses will not be significantly changed, and the algorithm was effective at achieving and maintaining the desired response in

hemoglobin as designed in the primary outcome (the algorithm will be subject to review and acceptance by FDA and other regulatory authorities). The algorithm was also designed to help minimize hemoglobin fluctuation and reduce the frequency of excessive excursions in hemoglobin. Only 4.3% of subjects receiving AKB-6548 had a hemoglobin excursion ³ 13.0 g/dL.

Patients were also analyzed for safety, including AEs, vital signs, electrocardiograms, and laboratory assay results. AKB-6548 was generally well tolerated with similar percentages of subjects experiencing adverse events in AKB-6548 treated and placebo groups. There was an increase in renal (kidney) related serious adverse events reported in the AKB-6548 treated subjects (AKB-6548 9.4% vs. placebo 2.8%), however, the number of subjects requiring dialysis, an objective measure of the severity of renal disease, was somewhat less in the AKB-6548 treated subjects (AKB-6548 8.0% vs. placebo 9.7%). Overall adverse events for renal and urinary disorders was balanced (AKB-6548 14.5% vs. placebo 13.9%). The disparity in renal serious adverse events was likely related to differences in reporting between investigators (reasons included proceeding to dialysis in association with a serious adverse event that was not reported in the renal category, or proceeding to dialysis without being considered a serious adverse event). Other differences, favoring either AKB-6548 or placebo, in adverse events were as follows: nausea and diarrhea (AKB-6548 10.1% vs. placebo 4.2%); gastrointestinal hemorrhage (AKB-6548 0.0% vs. placebo 5.6%); upper respiratory tract infection (AKB-6548 1.4% vs. placebo 6.9%); hyperkalemia (AKB-6548 5.1% vs. placebo 0.0%); and hypertension (AKB-6548 8.0% vs. placebo 2.8%). There were three deaths in AKB-6548 treated subjects. This was the expected number of subject deaths based on previous studies in similar populations.

Additional assessments conducted during our Phase 2b study include: iron metabolism (changes from baseline in iron, transferrin saturation (TSAT), TIBC, and ferritin); the dose of iron replacement needed to maintain iron levels; actual values and change from baseline in reticulocyte hemoglobin content, HbA1c, and lipids; functional biomarkers; concentration measurements of AKB-6548 and its glucuronide metabolite; and measures of patient reported outcomes. These will be reported in various scientific sessions in 2015, including the World Congress of Nephrology meeting in March 2015.

Ongoing and Planned Clinical Trials

Study of AKB-6548 in Dialysis Patients (CI-0011)

We are currently enrolling patients in a multiple dose, open label Phase 2 study in approximately 90 subjects (30 per cohort) on dialysis with anemia secondary to CKD. The primary endpoint will compare the change in hemoglobin from baseline for three different dosing regimens of AKB-6548: 1) 300 mg per dose administered once daily; 2) 450 mg administered once daily; and, 3) 450 mg administered three times per week. The first analysis of change in hemoglobin will be conducted at Week 8, and the second analysis at Week 16 will assess the change in hemoglobin with dose adjustment starting at Week 8. Key secondary endpoints will include (i) the safety of AKB-6548 in ESRD subjects on dialysis; (ii) the total dose of IV iron therapy for the eight weeks prior to baseline to the first (Weeks 1-8) and second (Weeks 9-16) eight weeks of treatment; and (iii) the effect of dialysis on the pharmacokinetics of AKB-6548. The first two cohorts (300 mg and 450 mg dose administered once daily, respectively) have been fully enrolled, and we have initiated enrollment in the third cohort. Thus far, dosing with AKB-6548 has been well tolerated. We plan to report the final results from this study in the third quarter of 2015 and to initiate Phase 3 studies for this indication in 2016.

Projected Phase 3 Clinical Trials

In the fourth quarter of 2014, we reported positive top-line results from a Phase 2b placebo-controlled study of AKB-6548 in non-dialysis patients with anemia related to chronic kidney disease (CKD). As a result, the company is planning meetings to discuss the Phase 2b study results with U.S. and European regulatory agencies in preparation for initiating global Phase 3 registration studies in 2015.

We are designing the Phase 3 program to be applicable for global development with limited protocol differences between geographic regions. We expect that two adequate and well controlled Phase 3 trials will be required to support the marketing application. The total number of patients to be enrolled in the Phase 3 studies will be determined upon agreement with FDA, EMA and other regulatory authorities.

We anticipate that one of the Phase 3 studies will be randomized, double-blind, and placebo-controlled enrolling CKD patients with anemia (hemoglobin < 10.5 g/dL). The primary endpoint would be to demonstrate non-inferiority for cardiovascular safety for AKB-6548 compared to the standard of care provided to the placebo group. The efficacy endpoint for this study will be to compare the ability to raise hemoglobin levels between AKB-6548 and placebo treatment groups. The study will include a rescue component for subjects with declining hemoglobin levels using injectable rESAs and/or transfusions in accordance with existing treatment guidelines (i.e. standard of care).

We expect that the second study will be a randomized, controlled, open-label study where subjects currently receiving treatment with rESAs are randomized 1:1 to receive AKB-6548 or to remain on their current rESA therapy. The primary efficacy endpoint would be to demonstrate non-inferiority for the mean change from the baseline hemoglobin level to the mean level during the evaluation period.

Although the exact size and timing cannot be known until final agreement is reached with the FDA, EMA and other regulatory authorities, we estimate that the two Phase 3 studies in non-dialysis patients with anemia related to CKD will include a total of approximately 3,000 - 3,500 subjects. We estimate that the cardiovascular safety study will be approximately 3 years in duration, with an average of 1.5 years on study drug.

Additional Studies

We have completed a thorough QT, or TQT, study in accordance with FDA guidance to ensure that AKB-6548 does not affect the cardiac conduction cycle (CI-0010). A lengthened QT interval is a biomarker for certain ventricular arrhythmias and a risk factor for sudden death. To date, AKB-6548 has not shown any tendency to affect the QT interval either in humans or animals. This study was a partially blinded, four way crossover study in 50 healthy volunteers, men and women. Each subject received the four different treatments (AKB-6548 600 mg, AKB-6548 1200 mg, Placebo, and Moxifloxacin 400 mg – each treatment taken at separate visits). The results from this study confirm that AKB-6548 does not alter cardiac repolarization intervals in healthy volunteers following a single dose of up to 1200 mg.

To test AKB-6548 in a chronic dosing setting, carcinogenicity assessments in two rodent species (rat and mouse) will be pursued. AKB-6548 has been shown to be orally bioavailable and pharmacologically active in both species. The results of a standard battery of tests that evaluate for mutations in cells or animals have indicated that AKB-6548 does not cause mutations that could lead to cancer. However, to satisfy the expected regulatory requirement, carcinogenicity assessments (two years of dosing in rats, and 6 months of dosing in a transgenic mouse model) in each of the two rodent species will be conducted. Completion of three-month (mouse; ongoing) and six-month (rat; completed) oral toxicity evaluations will support dose selection for the respective carcinogenicity assessment.

Finally, in order to complete the registration package for drug approval, we are exploring the need to evaluate specific drug interactions with patients taking AKB-6548, as patients with CKD take multiple medications. It is likely we will conduct at least one of these additional clinical studies.

AKB-6899

AKB-6899 is also a HIFa-stabilizing compound. In screening AKB-6899 for its HIF-related properties, it was discovered that in cells cultured at low oxygen levels, AKB-6899 significantly inhibited the expression of VEGF and phosphoglycerate kinase, or PGK, mRNA, both of which are associated with the growth of cancerous tumors. In addition, AKB-6899 was found to significantly stimulate the production of soluble vascular endothelial growth factor receptor 1, or sVEGFr1. sVEGFr1 is known to be a potent inhibitor of VEGF signaling by sequestering VEGF and inhibiting its interaction with transmembrane receptors—in so doing, sVEGFr1 can inhibit the growth of certain types of cancer cells. AKB-6899 was also found to stimulate the production of EPO in a manner similar to AKB-6548.

These properties, and others, indicate that AKB-6899 may be an effective treatment for certain cancers (ovarian, breast, colon, and possibly lung), alone or in combination with chemotherapy. In addition AKB-6899 may also be a candidate compound for the treatment of chemotherapy-induced anemia and for VEGF-related eye diseases. AKB-6899 has been used effectively in several animal models of cancer, both alone and in combination. In addition, it has been shown to be effective in animal models of colitis.

Manufacturing and Supply

AKB-6548 is a small-molecule drug that is manufactured from readily available commercial starting materials. The manufacturing of AKB-6548 uses standard chemical technologies and equipment, and more than 440kg of drug substance has been manufactured to date. The intended commercial manufacturing route has been successfully transferred to Evonik Corporation for large-scale manufacture of AKB-6548.

The drug substance can be readily formulated into compressed tablets using common manufacturing processes employing standard USP grade excipients. Compressed tablets have been made of different potencies with excellent tabletting properties (i.e. hardness, disintegration time and friability) and a fast, reproducible dissolution rate.

AKB-6899 is at the pre-clinical stage. A scalable manufacturing route has been developed for the drug substance of AKB-6899. Thus far, 2kg of non-GMP material and 10kg of GMP material has been successfully manufactured.

We have no internal manufacturing capabilities and rely on outside manufacturers to produce all lots of drug substance and drug products. On February 28, 2014, we entered into a Master Services Agreement with Evonik Corporation, or Evonik, pursuant to which Evonik shall further develop and manufacture the drug substance for use in our Phase 3 development program for AKB-6548 and other clinical trials.

On June 24, 2014, we entered into a Master Services Agreement with Gregory Pharmaceutical Holdings, Inc. (d/b/a UPM Pharmaceuticals Inc., or UPM), pursuant to which UPM shall further develop and manufacture the drug product for use in our Phase 3 development program for AKB-6548 and other clinical trials.

AKB-6548 has been manufactured under strict cGMP regulations and we believe has fully complied with the FDA guidelines for the manufacture of drug substance and drug product used in clinical trials.

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 U.S. and foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development and implementation of our business. We also rely on know-how, continuing technological innovation and potential in-licensing opportunities to develop and maintain our proprietary position. Additionally, we may benefit from a variety of statutory frameworks in the United States, Europe and other countries that provide periods of non-patent-based exclusivity for qualifying molecules. See “—Regulatory Matters.”

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

Our patent estate, on a worldwide basis, includes 56 allowed applications and issued patents and approximately 45 pending utility and provisional patent applications, with pending and issued claims relating to our current clinical stage candidate AKB-6548 as well as other product candidates, including AKB-6899. We also hold three patents that claim the crystal of a protein-ligand complex of EGLN-1 as well as methods for identifying compounds that bind to EGLN-1.

Individual patents extend for varying periods of time depending on the date of filing of the patent application or the date of patent issuance and the legal term of patents in the countries in which they are obtained. Generally, patents issued from applications filed in the United States are effective for twenty years from the earliest non-provisional filing date. In addition, in certain instances, a patent term can be extended to recapture a portion of the term effectively lost as a result of the FDA regulatory review period, however, the restoration period cannot be longer than five years and the total patent term including the restoration period must not exceed 14 years following FDA approval. The duration of foreign patents varies in accordance with provisions of applicable local law, but typically is also twenty years from the earliest international filing date. 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 AKB-6548, dosing regimens, formulations, and various other aspects relating to the treatment of anemia using AKB-6548 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.

AKB-6548 Patent Portfolio

We hold five issued patents and one pending application covering the composition of matter, method of treating anemia, and pharmaceutical compositions of AKB-6548 in the United States, one issued patent in Europe (registered in most countries of the European Patent Convention), and additional patents issued or pending in many other major jurisdictions worldwide, including Japan, China, South Korea, Brazil, Mexico, Russia, Israel and India. The expected expiration date for these composition of matter patents is 2028 plus any extensions or adjustments of term available under national law.

In July of 2011, a third party filed an opposition to our issued European Patent No. 2044005 (the ’005 Patent). During the oral proceedings, which took place on April 10, 2013, the Opposition Division of the European Patent Office maintained the ‘005 Patent on the basis of the third auxiliary request filed during the oral proceedings. This decision resulted in the maintenance of a claim directed to a compound chosen from a group of eight compounds, including AKB-6548, as well as claims to compositions and methods for treating various diseases, including, but not limited to, anemia. Both parties have appealed the decision of the Opposition

Division and final resolution of the opposition proceedings will likely take a number of years. We cannot be assured of the breadth of the claims that will remain in the ’005 Patent or that the patent will not be revoked in its entirety.

We also hold patents and patent applications directed to processes for manufacturing AKB-6548, dosing regimens, formulations, polymorphs, and various other aspects relating to the treatment of anemia using AKB-6548 that are expected to expire between 2032 and 2034 exclusive of possible patent term extensions.

AKB-6899 Patent Portfolio

We hold four issued patents and one pending application covering the AKB-6899 composition of matter and pharmaceutical compositions or methods of use in the United States, and additional patents issued or pending in many other major jurisdictions worldwide, including Europe, Japan, China, South Korea, Brazil, Mexico, Russia and India. The expected expiration date for these composition of matter patents is 2028 plus any extensions or adjustments of term available under national law.

We hold one issued patent that covers the treatment of anemia by administration of AKB-6899, which is expected to expire in 2028. We also hold, either alone or jointly, one issued patent and one pending application covering various methods, including, but not limited to, the treatment of cancer by administration of AKB-6899 in the United States and additional patent applications are pending in many other major jurisdictions worldwide, including Japan, China, South Korea, Mexico, Russia, Israel and India. The expected expiration dates for these method of treatment patent applications are expected to be 2032 exclusive of possible patent term extensions or adjustments. We hold one pending PCT patent application directed to treatment or prevention of ocular conditions using AKB-6899, and one pending PCT patent application directed to dosing regimens of AKB-6899. The expected expiration date of this ocular patent application is 2035, and the expected expiration date of this dosing patent application is 2034, exclusive of possible patent term extensions or adjustments. We also hold one pending patent application directed to polymorphs of AKB-6899 in the United States and various foreign jurisdictions. The expected expiration date of this polymorph patent application is 2034 exclusive of possible patent term extensions or adjustments.

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 U.S. patents issued to 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 U.S. patents conflict with our intellectual property rights; nor do we make any admission that any of such patents are valid or enforceable. Under U.S. 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 U.S. 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.

In addition, we are aware of certain foreign patents owned by FibroGen. For example, in June 2013, the European Patent Office granted European Patent No. 1463823 (the ’823 patent) to FibroGen. The ’823 patent claims, among other things, the use of a heterocyclic carboxamide compound selected from the group consisting of pyridine carboxamides, quinoline carboxamides, isoquinoline carboxamides, cinnoline carboxamides, and beta-carboline carboxamides that inhibits HIF-PH enzyme activity in the manufacture of a medicament for increasing endogenous EPO in the prevention, pretreatment, or treatment of anemia. On December 5, 2013, we filed an opposition with the European Patent Office to the ’823 patent requesting that the ’823 patent be revoked in its entirety. While, for the reasons set forth in our opposition, we believe the ’823 patent should be revoked in its entirety, the ultimate outcome of the opposition remains uncertain.

Competition

We operate in highly competitive segments of the biotechnology and biopharmaceutical markets. We face competition from many different sources, including commercial pharmaceutical and biotechnology enterprises, academic institutions, government agencies and private and public research institutions. Many of our competitors have significantly greater financial, product development, manufacturing and marketing resources than us. Large pharmaceutical companies have extensive experience in clinical testing and obtaining regulatory approval for drugs. These companies also have significantly greater research capabilities than us. Many universities and private and public research institutes are active in CKD research, some in direct competition with us. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. The key competitive factors affecting the success of AKB-6548, if approved, are likely to be its efficacy, convenience and safety profile.

If AKB-6548 is approved and launched commercially, competing drugs will include EPOGEN and potentially Aranesp, which are both marketed by Amgen, Inc., or Amgen, in addition to Procrit and Eprex, which are marketed by Johnson & Johnson. Aranesp, introduced in 2001, has significant market share in the United States, particularly in the oncology and the non-dialysis markets, although it is approved for treatment in dialysis patients as well. In Europe, Roche has obtained regulatory approval to market, and has launched, a PEGylated rESA called Mircera. Mircera reportedly has greater plasma stability than any of the currently marketed products. PEG is a polymer that increases the time rEPO remains in the circulation and consequently can be dosed less frequently. Mircera has also obtained regulatory approval in the United States, but as a result of Roche and Amgen’s patent infringement litigation, Mircera was found to infringe several U.S. patents owned by Amgen and has been enjoined from being sold in the United States until mid-2014 under the terms of a limited license. If Mircera enters the U.S. market, we believe it will be in direct competition with AKB-6548 because of Mircera’s ability to be long-acting; therefore, it could potentially limit the market for AKB-6548.

We may also face competition from potential new anemia therapies if we obtain approval for and commercially launch AKB-6548. There are several other HIF product candidates for anemia indications in various stages of development by potential competitors. These candidates are being developed by companies such as FibroGen in partnership with AstraZeneca PLC in the United States and China and with Astellas Pharma Inc., in Europe and Asia, Japan Tobacco, GlaxoSmithKline and Bayer, all of whom are likely to have greater financial resources than our

company. FibroGen, in particular, is ahead of us in the clinical development of its product, FG-4592 (roxadustat). Such HIF compounds under development may have a mechanism of action that is the same or similar to AKB-6548 and promote the production of naturally occurring EPO in patients. Some of these product candidates may enter the market in advance of AKB-6548. If these product candidates enter the market, they may compete with AKB-6548, if it is approved and marketed.

In addition, certain companies are developing potential new therapies for renal-related diseases that could potentially reduce rESA utilization and thus limit the market for AKB-6548 if it is approved and marketed.

The introduction of biosimilars into the rEPO market in the United States will constitute additional competition for AKB-6548 if it is approved and marketed. A biosimilar product is a subsequent version of an existing, branded biologic product. The patent for the existing, branded product must expire in a given market before biosimilars may enter that market. The patents for epoetin alfa, a version of rEPO, expired in 2004 in the European Union, and the remaining patents have expired or will expire in 2012 through 2015 in the United States. Several biosimilar versions of rEPO are available for sale in the European Union and biosimilar versions of rEPO are currently being studied in clinical trials in the United States.

In February 2015, Hospira announced that it submitted a Biologics License Application (BLA) to the FDA on December 16, 2014, for Retracrit, a proposed biosimilar to epoeitin alfa. In October 2012, Sandoz announced the beginning of its Phase 3 clinical program for its biosimilar rEPO with results anticipated in 2014. Upon entry into the U.S. market, biosimilars will compete with AKB-6548 if it is approved and marketed, and will likely drive down prices for rEPO, which could also adversely affect our reimbursement.

In the dialysis market, it is typical to compete for and enter into long-term supply agreements with the major operators of dialysis clinics in the United States. In particular, two of the largest operators of dialysis clinics in the United States, DaVita Inc., or DaVita, and Fresenius, account for more than half of the rESA sales in the U.S. dialysis market. Both DaVita and Fresenius entered into a long-term supply agreements with Amgen, Inc. that began in January 2012. We believe that it may be challenging to enter into or expand upon long or short-term supply agreements with DaVita, Fresenius or other operators of dialysis clinics.

Regulatory Matters

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

U.S. Government Regulation

In the United States, the FDA regulates drug products under the Federal Food, Drug, and Cosmetic Act, or FFDCA, and the FDA's implementing regulations. If we fail to comply with applicable FDA or other requirements at any time during the drug development process, clinical testing, the approval process or after approval, we may become subject to administrative or judicial sanctions. These sanctions could include the FDA's refusal to approve pending applications, license suspension or revocation, withdrawal of an approval, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties or criminal prosecution. Any FDA enforcement 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 nonclinical laboratory tests, nonclinical 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 IND application which must become effective before human clinical trials in the United States may begin;
- approval by an IRB or ethics committee at each clinical trial site 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 an NDA;

- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with current cGMP regulations;

- satisfactory completion of a potential review by an FDA advisory committee, if applicable; and

- FDA review and approval of the NDA prior to any commercial marketing, sale or commercial shipment of the drug in the United States.

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

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

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

A sponsor who wishes to conduct a clinical trial outside the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the sponsor may submit data from the clinical trial to the FDA in support of an NDA so long as the clinical trial is conducted in compliance with an international guideline for the ethical conduct of clinical research known as the Declaration of Helsinki, as set out in the FDA regulations or 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.

Clinical Trials

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

- Phase 1: Clinical trials are initially conducted in a limited population of subjects to test the drug candidate for safety, dose tolerance, absorption, metabolism, distribution and excretion in healthy humans or, on occasion, in patients with severe problems or life threatening diseases to gain an early indication of its effectiveness.

- Phase 2: Clinical trials are generally conducted in a limited patient population to evaluate dosage tolerance and appropriate dosage, identify possible adverse effects and safety risks, and evaluate preliminarily the efficacy of the drug for specific targeted indications in patients with the disease or condition under study.

- Phase 3: Clinical trials are typically conducted when Phase 2 clinical trials demonstrate that a dose range of the product candidate is effective and has an acceptable safety profile. Phase 3 clinical trials are commonly referred to as “pivotal” studies, which typically denotes a study which presents the data that the FDA or other relevant regulatory agencies will use to determine whether or not to approve a drug. Phase 3 clinical trials are generally undertaken with large numbers of patients, such as groups of several hundred to several thousand, to further evaluate dosage, to provide substantial evidence of clinical efficacy and to further test for safety in an expanded and diverse patient population at multiple, geographically-dispersed clinical trial sites.

- Phase 4: In some cases, FDA may condition approval of an NDA for a product candidate on the sponsor's agreement to conduct additional clinical trials after NDA approval. In other cases, a sponsor may voluntarily conduct additional clinical trials post-approval to gain more information about the drug. Such post approval trials are typically referred to as Phase 4 clinical trials.

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

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 and purity 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 shelf life.

New Drug Applications

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

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

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

After the FDA evaluates the NDA and conducts inspections of manufacturing facilities, it may issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the application is not ready for approval. A Complete Response Letter 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 REMS to mitigate risks, which could include medication guides, physician communication plans, or elements to ensure safe use, such as restricted distribution programs, patient registries or other risk minimization tools. The FDA may also condition approval on, among other things, changes to proposed labeling, development of adequate controls and specifications, or a commitment to conduct one or more post-market studies or clinical trials. Such post-market testing may include Phase 4 clinical trials and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

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 require a recall of any drug already on the market. In addition, the FDA has the authority to prevent or limit further marketing of a drug based on the results of post-market studies or surveillance programs.

After regulatory approval of a drug is obtained, companies are subject to a number of post-approval requirements. For example, there are reporting obligations regarding certain adverse events received and production problems. Companies are also required to report updated safety and efficacy information and to comply with requirements concerning advertising and promotional labeling. Drugs may be marketed only for the FDA approved indications and in accordance with the provisions of the approved labeling. The FDA closely regulates the post-approval marketing and promotion of drugs, including standards and regulations for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the Internet. A company

can make only those claims relating to safety and efficacy that are approved by the FDA. Failure to comply with these requirements can result in adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available drugs for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, impose stringent restrictions on manufacturers' communications regarding off-label use.

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

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

Special Protocol Assessment

An SPA is a written agreement with the FDA on the details of the design, size, execution and planned analysis for a clinical trial intended to form the primary basis of an effectiveness claim in an NDA. After the clinical trial begins, the agreement may only be changed through a written agreement between the sponsor and the FDA. An SPA is generally binding upon the FDA unless the FDA determines that there are public health concerns unrecognized at the time the SPA agreement was entered into, other new scientific concerns regarding product safety or efficacy arise, or if the sponsor fails to comply with the agreed-upon trial protocol, or standard-of-care changes such that FDA does not accept that the trial comparator is accurate to assess the results from the trial. If the outcome of the clinical trial is successful, the sponsor will ordinarily be able to rely on it as the primary basis for approval with respect to effectiveness. FDA requires 45 days to review each SPA and often 2-3 review cycles may be necessary to reach written agreement between FDA and the sponsor. Any protocol amendment during the conduct of the clinical trial may invalidate the SPA agreement, requiring a submission of the amended protocol to the FDA for additional review and revision of the initial agreement. FDA has 45 days to review each requested amendment to an issued SPA. Failure of the sponsor to comply with the written SPA agreement could affect approvability of the NDA.

Europe/Rest of World Government Regulation

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

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

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

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

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

Fraud and Abuse Laws

In the United States, the research, manufacturing, distribution, sale and promotion of drug products and medical devices are subject to regulation by various federal, state and local authorities in addition to the FDA, including the CMS, other divisions of the U.S. Department of Health and Human Services (e.g., the Office of Inspector General), the U.S. Department of Justice, state Attorneys General, and other state and local government agencies.

These laws include the federal Anti-Kickback Statute, which makes it illegal for any person, including a prescription drug manufacturer (or a party acting on its behalf) to knowingly and willfully solicit, receive, offer, or pay any remuneration that is intended to induce the referral of business, including the purchase, order, or prescription of a particular drug, for which payment may be made under a federal healthcare program, such as Medicare or Medicaid. Violations of this law are punishable by up to five years in prison, criminal fines, administrative civil money penalties, and exclusion from participation in federal healthcare programs. In addition, the PPACA, among other things, amends the intent requirement of the federal Anti-Kickback Statute and criminal healthcare fraud statutes created by HIPAA. A person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it. Moreover, the PPACA provides that the government may assert that a claim including items or services resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim for purposes of the False Claims Act.

Although we would not submit claims directly to payors, drug manufacturers can be held liable under the federal False Claims Act, which prohibits anyone from knowingly presenting, or causing to be presented, for payment to federal programs (including Medicare and Medicaid) claims for items or services, including drugs, that are false or fraudulent, claims for items or services not provided as claimed, or claims for medically unnecessary items or services. The government may deem manufacturers to have "caused" the submission of false or fraudulent claims by, for example, providing inaccurate billing or coding information to customers or promoting a product off-label. In addition, our future activities relating to the reporting of wholesaler or estimated retail prices for our products, the reporting of prices used to calculate Medicaid rebate information and other information affecting federal, state, and third-party reimbursement for our products, and the sale and marketing of our products, are subject to scrutiny under this law. Penalties for a False Claims Act violation include three times the actual damages sustained by the government, plus mandatory civil penalties of between $5,500 and $11,000 for each separate false claim, the potential for exclusion from participation in federal healthcare programs, and, although the federal False Claims Act is a civil statute, conduct that results in a False Claims Act violation may also implicate various federal criminal statutes. If the government were to allege that we were, or convict us of, violating these false claims laws, we could be subject to a substantial fine and may suffer a decline in our stock price. In addition, private individuals have the ability to bring actions under the federal False Claims Act and certain states have enacted laws modeled after the federal False Claims Act.

In addition to the laws described above, the PPACA also imposed new reporting requirements on drug manufacturers for payments made to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Failure to submit required information may result in civil monetary penalties of up to an aggregate of $150,000 per year (or up to an aggregate of $1 million per year for "knowing failures"), for all payments, transfers of value or ownership or investment interests that are not timely, accurately and completely reported in an annual submission. Drug manufacturers were required to begin collecting data on August 1, 2013 and will be required to submit reports to CMS by March 31, 2014 (and by the 90th day of each subsequent calendar year).

In addition, many states have adopted laws similar to the federal laws discussed above. Some of these state prohibitions apply to the referral of patients for healthcare services reimbursed by any insurer, not just federal healthcare programs such as Medicare and Medicaid. There has also been a recent trend of increased federal and state regulation of payments made to physicians. Certain states mandate implementation of compliance programs, impose restrictions on drug manufacturers' marketing practices and/or require the tracking and reporting of gifts, compensation and other remuneration to physicians. Because we intend to commercialize products that could be reimbursed under a

federal healthcare program and other governmental healthcare programs, we plan to develop a comprehensive compliance program that establishes internal controls to facilitate adherence to the rules and program requirements to which we will or may become subject. Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Due to the breadth of and ambiguities in these laws, the absence of guidance in the form of regulations or court decisions, and the potential for additional legal or regulatory change in this area, it is possible that our future sales and marketing practices and/or our future relationships with physicians might be challenged under these laws. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business.

Third-Party Coverage and Reimbursement

Sales of pharmaceutical products depend in significant part on the availability of coverage and adequate reimbursement by third-party payors, such as state and federal governments, including Medicare and Medicaid, and commercial managed care providers. In the United States, no uniform policy of coverage and reimbursement for drug products exists among third-party payors. Accordingly, decisions regarding the extent of coverage and amount of reimbursement to be provided for AKB-6548 will be made on a payor by payor basis. As a result, the coverage determination process is often a time-consuming and costly process that will require us 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. Third-party payors may limit coverage to specific drug products on an approved list, or formulary, which might not include all of the FDA-approved drugs for a particular indication. A decision by a third-party payor not to cover our product candidates could reduce physician utilization of our products once approved and have a material adverse effect on our future sales, results of operations and financial condition. Moreover, a payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

Healthcare Reform

In March 2010, the PPACA was enacted, which includes measures that have or will significantly change the way health care is financed by both governmental and private insurers. Among the provisions of PPACA of greatest importance to the pharmaceutical industry are the following:

- Effective in 2010, PPACA made several changes to the Medicaid Drug Rebate Program, including increasing pharmaceutical manufacturers' rebate liability by raising the minimum basic Medicaid rebate on most branded prescription drugs and biologic agents from 15.1% of average manufacturer price, or AMP, to 23.1% of AMP and adding a new rebate calculation for "line extensions" (i.e., new formulations, such as extended release formulations) of solid oral dosage forms of branded products, as well as potentially impacting their rebate liability by modifying the statutory definition of AMP.

- PPACA also expanded the universe of Medicaid utilization subject to drug rebates by requiring pharmaceutical manufacturers to pay rebates on Medicaid managed care utilization as of 2010 and by expanding the population potentially eligible for Medicaid drug benefits, to be phased-in by 2014. CMS has proposed to expand Medicaid rebate liability to the territories of the United States as well.

- In addition, PPACA provides for the public availability of retail survey prices and certain weighted average AMPs under the Medicaid program. The implementation of this requirement by the CMS may also provide for the public availability of pharmacy acquisition cost data, which could negatively impact our sales.

- Effective in 2010, PPACA expanded the types of entities eligible to receive discounted 340B pricing, although, under the current state of the law, with the exception of children's hospitals, these newly eligible entities will not be eligible to receive discounted 340B pricing on orphan drugs when used for the orphan indication. In addition, as 340B drug pricing is determined based on AMP and Medicaid rebate data, the revisions to the Medicaid rebate formula and AMP definition described above could result in an increase in the required 340B discounts.

- Effective in 2011, PPACA imposed a requirement on manufacturers of branded drugs and biologic agents to provide a 50% discount off the negotiated price of branded drugs dispensed to Medicare Part D patients in the coverage gap (i.e., "donut hole").

- Effective in 2011, PPACA imposed an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, although this fee would not apply to sales of certain products approved exclusively for orphan indications.

- As of 2010, a new Patient-Centered Outcomes Research Institute was established pursuant to PPACA to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research. The research conducted by the Patient-Centered Outcomes Research Institute may affect the market for certain pharmaceutical products.

- PPACA created the Independent Payment Advisory Board which, beginning in 2014, will have authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription drugs. Under certain circumstances, these recommendations will become law unless Congress enacts legislation that will achieve the same or greater Medicare cost savings.

- PPACA established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending. Funding has been allocated to support the mission of the Center for Medicare and Medicaid Innovation from 2011 to 2019.

Many of the details regarding the implementation of PPACA are yet to be determined and, at this time, it remains unclear the full effect that PPACA would have on our business. In addition, we expect that additional state and federal healthcare reform measures will be adopted in the future. Because we anticipate that a significant proportion of patients eligible for AKB-6548 will be covered by Medicare Part D, any government healthcare reform measures which limit the amounts that federal and state governments will pay for healthcare products and services could result in reduced demand for our products once approved or additional pricing pressures.

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, 2014, we had 43 employees, 41 of whom were full-time, 12 of whom hold Ph.D. or M.D. degrees, 19 of whom were engaged in research and development activities and 24 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 15,367 square feet of office space in Cambridge, Massachusetts under a lease that expires on December 31, 2016. 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 1A. Risk Factors
Risk Factors

The following risk factors and other information included in this Annual Report on Form 10-K should be carefully considered. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently believe to be immaterial may also adversely affect our business. Please reference our "Cautionary Note Regarding Forward-Looking Statements," which identifies certain forward-looking statements contained in this report that are qualified by these risk factors. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected.

Risks Related to our Financial Position and Need for Additional Capital

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

We have incurred net losses each year since our inception, including net losses of $37.0 million for the year ended December 31, 2014, and $13.2 million for the year ended December 31, 2013. As of December 31, 2014, we had an accumulated deficit of $100.7 million. To date, we have not commercialized any products or generated any revenue from the sale of products, and we do not expect to generate any product revenue in the foreseeable future. We do not know whether or when we will generate revenue or become profitable.

We have devoted most of our financial resources to research and development, including our clinical and preclinical development activities. To date, we have financed our operations primarily through our initial public offering, or IPO, and private placements of our preferred stock. 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, strategic collaborations or grants. Our lead product candidate, AKB-6548, has recently completed a Phase 2b study, and our other product candidate is in preclinical development. Therefore, we expect that it will be several years, if ever, before we have a product candidate ready for commercialization. Even if we obtain regulatory approval to market AKB-6548, our future revenue will depend upon the size of any markets in which AKB-6548 has received approval, our ability to achieve sufficient market acceptance, the availability and extent of reimbursement from third-party payors and other factors.

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

- continue our Phase 2 clinical development of AKB-6548 for the treatment of anemia in patients undergoing dialysis and prepare for and initiate a Phase 3 development program of AKB-6548 for the treatment of anemia secondary to CKD in patients not on dialysis;
- seek regulatory approvals for our product candidates that successfully complete clinical studies;
- have our product candidates manufactured for clinical trials and for commercial sale;
- establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval;
- initiate additional preclinical, clinical or other studies for additional indications for AKB 6548, AKB 6899 and other product candidates that we may develop or acquire;
- seek to discover and develop additional product candidates;
- acquire or in-license other commercial products, product candidates and technologies;
- make royalty, milestone or other payments under any future in-license agreements;
- maintain, protect and expand our intellectual property portfolio;

attract and retain skilled personnel; and

continue to create additional infrastructure to support our operations as a public company.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, if at all, we will be able to achieve profitability. If we are required by the United States Food and Drug Administration, or FDA, the European Medicines Agency, or EMA, or other regulatory authorities to perform studies in addition to or larger than those currently expected, or if there are any delays in completing our clinical trials or the development of any of our product candidates, our expenses could increase.

The net losses we incur may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance. In any particular quarter or quarters, our operating results could be below the expectations of securities analysts or investors, which could cause our stock price to decline.

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

Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable could depress the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product offerings or even continue our operations. A decline in the value of our company could cause our shareholders to lose all or part of their investment.

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

As of December 31, 2014, our cash and cash equivalents and available for sale securities were $108.9 million. We believe that we will continue to expend substantial resources for the foreseeable future developing AKB-6548, AKB-6899 and any other product candidates that we may develop or acquire. These expenditures will include costs associated with research and development, potentially obtaining regulatory approvals and having our products manufactured, as well as marketing and selling products approved for sale, if any. In addition, other unanticipated costs may arise. Because the outcome of our current and anticipated clinical trials is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of our product candidates.

Our future capital requirements depend on many factors, including:

the rate of progress of, results of and cost of completing Phase 2 clinical development of AKB-6548 for the treatment of anemia in patients undergoing dialysis;
the results of our meetings with the FDA and the EMA and other regulatory authorities and the consequential effect on our operating costs;
assuming AKB-6548 advances to Phase 3 clinical studies, the scope, size, rate of progress, results and costs of initiating and completing our Phase 3 development program of AKB-6548;
assuming favorable Phase 3 clinical results, the cost, timing and outcome of our efforts to obtain marketing approval for AKB-6548 in the United States, Europe and in other jurisdictions, including to fund the preparation and filing of regulatory submissions for AKB-6548 with the FDA, the EMA and other regulatory authorities;
the scope, progress, results and costs of additional preclinical, clinical, or other studies for additional indications for AKB-6548, AKB-6899 and other product candidates that we may develop or acquire;

the timing of, and the costs involved in, obtaining regulatory approvals for AKB-6899 if clinical studies are successful;
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;
the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval;
the cost of having our product candidates manufactured for clinical trials and in preparation for commercialization;
our ability to establish and maintain strategic collaborations, licensing or other arrangements and the financial terms of such agreements;
the costs involved in preparing, filing and prosecuting patent applications and maintaining, defending and enforcing our intellectual property rights, including litigation costs, and the outcome of such litigation; and
the extent to which we acquire or in-license other products or technologies.

Based on our current operating plan, and absent any future financings or strategic partnerships, we believe that the net proceeds we received from our IPO, and our existing cash and cash equivalents and available for sale securities, will be sufficient to fund our projected operating expenses and capital expenditure requirements through the first half of 2016. However, our operating plan may

change as a result of many factors currently unknown to us, and we may need additional funds sooner than planned. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. Additional funds may not be available when we need them on terms that are acceptable to us, or at all. If adequate funds are not available to us on a timely basis, we may be required to delay, limit, reduce or terminate preclinical studies, clinical trials or other development activities for AKB-6548, AKB-6899 or any other product candidates that we develop or acquire, or delay, limit, reduce or terminate our establishment of sales and marketing capabilities or other activities that may be necessary to commercialize our product candidates.

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

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings and license, development and commercialization agreements with collaborators. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of our common stockholders will be diluted, and the terms may include liquidation or other preferences and anti-dilution protections that adversely affect the rights of our common stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take certain actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through strategic collaborations with third parties, we may have to relinquish valuable rights to our product candidates, future revenue streams, research programs or product candidates or grant licenses on terms that are not favorable to us. If we are unable to raise additional funds through equity or debt financing when needed, we may be required to delay, limit, reduce or terminate our product development or commercialization efforts for AKB-6548, AKB 6899 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.

Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

We commenced active operations in 2007, and our operations to date have been limited to organizing and staffing our company, business planning, raising capital, identifying potential product candidates, undertaking preclinical studies and conducting clinical trials. We currently have two product candidates, one of which is in preclinical development. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. Only a small percentage of biopharmaceutical development programs ultimately result in commercial products or even product candidates and a number of events could delay our development efforts and negatively impact our ability to obtain regulatory approval for, and to manufacture, market and sell, a biopharmaceutical product. We have not yet demonstrated our ability to successfully complete later stage clinical trials, obtain regulatory approvals, manufacture a commercial scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization.

In addition, as a relatively young business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We will need to expand our capabilities to support commercial activities. We may not be successful in adding such capabilities.

Risks Related to our Business and the Clinical Development, Regulatory Review and Approval of AKB-6548 and AKB-6899

We depend heavily on the success of one product candidate, AKB-6548, which just completed a Phase 2b study. Even if we obtain favorable clinical results in our Phase 3 studies, we may not be able to obtain regulatory approval for, or successfully commercialize, AKB-6548.

We currently have only one product candidate, AKB-6548, in clinical development, and our business depends almost entirely on the successful clinical development, regulatory approval and commercialization of that product candidate, which may never occur. We currently have no drug products for sale, generate no revenue from sales of any drugs, and may never be able to develop marketable drug products. AKB-6548, which has completed a Phase 2b study, will require substantial additional clinical development, testing, manufacturing process development, and regulatory approval before we are permitted to commence its commercialization. Our other product candidate, AKB-6899, is in preclinical development. None of our product candidates has advanced into a pivotal study, and it may be years before any such study is initiated. 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 intend to test and, if approved, market any product candidates. Before obtaining regulatory approval for the commercial sale of any product candidate, we must demonstrate through extensive preclinical testing and clinical trials that the product candidate is safe and effective for use in each target indication. This process can take many years. Of the large number of drugs in development in the United States, only a small percentage successfully complete the FDA regulatory

approval process and are commercialized. Accordingly, even if we are able to obtain the requisite capital to continue to fund our development and clinical programs, we may be unable to successfully develop or commercialize AKB-6548.

We are not permitted to market AKB-6548 in the United States until we receive approval from the FDA, or in any jurisdiction outside of the United States until we receive the requisite approval from such jurisdiction. As a condition to submitting a New Drug Application, or NDA, to the FDA for AKB-6548 regarding its ability to treat patients with anemia secondary to CKD, we must complete Phase 3 studies and any additional non-clinical or clinical studies required by the FDA. AKB-6548 may not be successful in clinical trials or receive regulatory approval. Further, AKB-6548 may not receive regulatory approval even if it is successful in clinical trials. Obtaining approval of an NDA is a complex, lengthy, expensive and uncertain process that typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, the safety concerns associated with injectable rESAs and the black box warnings in their prescribing information may affect the FDA's review of the safety results of AKB-6548. Further, the policies or regulations, or the type and amount of clinical data necessary to gain approval, may change during the course of a product candidate's clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any product candidate and it is possible that AKB-6548 will never obtain regulatory approval. The FDA may delay, limit or deny approval of AKB-6548 for many reasons, including, among others:

- we may not be able to demonstrate that AKB-6548 is safe and effective in treating anemia secondary to CKD to the satisfaction of the FDA;
- the results of our clinical trials may not meet the level of statistical or clinical significance required by the FDA for marketing approval;
- the FDA may disagree with the number, design, size, conduct or implementation of our clinical trials;
- the FDA may not approve the formulation, labeling or specifications we request for AKB-6548;
- the FDA may approve AKB-6548 for use only in a small patient population;
- the FDA may require that we conduct additional clinical trials;
- the clinical research organizations, or CROs, that we retain to conduct our clinical trials may take actions outside of our control that materially adversely impact our clinical trials;
- we may fail to perform in accordance with the FDA's good clinical practice, or GCP, requirements;
- the FDA may disagree with inclusion of patients from certain regions outside the United States to support the NDA for potential reasons such as differences in clinical practice from United States standards;
- the FDA may disagree with our interpretation of data from our nonclinical studies and clinical trials;
- the FDA may not approve the manufacturing processes or facilities of third-party manufacturers with whom we contract; or
- the policies or regulations of the FDA may significantly change in a manner that renders our clinical data insufficient for approval, or requiring that we amend or submit new clinical protocols.

In addition, similar reasons may cause the EMA or other regulatory authorities to delay, limit or deny approval of AKB-6548 outside the United States.

Any of these factors, many of which are beyond our control, could jeopardize our ability to obtain regulatory approval for and successfully market AKB-6548. Because our business is almost entirely dependent upon AKB-6548, any such setback in our pursuit of regulatory approval would have a material adverse effect on our business and prospects.

Alternatively, even if we obtain regulatory approval, that approval may be for indications or patient populations that are not as broad as we intend or desire or may require labeling that includes significant use or distribution restrictions or safety warnings. We may also be required to perform additional, unanticipated clinical trials to obtain approval or be subject to additional post-marketing testing requirements to maintain regulatory approval. In addition, regulatory authorities may withdraw their approval of a product or the FDA may require a risk evaluation and mitigation strategy, or REMS, for a product, which could impose restrictions on its distribution. Any of the foregoing scenarios could materially harm the commercial prospects for AKB-6548 or our other product candidates.

We have not obtained agreement with the FDA, EMA or other regulatory authorities on the design of our Phase 3 development program.

Although we have recently completed our Phase 2b study, we have not obtained agreement with the FDA on the design of our Phase 3 development program. We plan to hold an end of Phase 2 meeting with the FDA in 2015 and if the FDA determines that the Phase 2b

study results do not support moving into a pivotal program, we would be required to conduct additional Phase 2 studies. Alternatively, the FDA could disagree with the proposed design of our Phase 3 development program and could suggest a larger number of subjects or a longer course of treatment than our current expectations. If the FDA takes such positions, the costs of our AKB-6548 development program could increase materially, and the potential market introduction of AKB-6548 could be delayed or we could risk not obtaining FDA approval even if the Phase 3 trials meet their primary endpoints. The FDA also may require that we conduct additional clinical, nonclinical or manufacturing validation studies and submit that data before it will consider an NDA.

We have not yet received formal scientific advice on the regulatory path for AKB-6548 from the EMA or other regulatory authorities. We cannot predict what additional requirements may be imposed by these regulatory authorities or how such requirements might delay or increase costs for our planned Phase 3 development program. Because our business is almost entirely dependent upon the successful development, regulatory approval, and commercialization of AKB-6548, any such delay or increase in costs would have an 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 for AKB-6548 because of concerns from adverse events observed with injectable rESAs, other investigational agents and commercial products in CKD or for other reasons, including competitive clinical studies for similar patient populations. In addition, patients controlling their disease with injectable rESAs may be reluctant to participate in a clinical trial with an investigational drug. Finally, competition for clinical trial sites may limit our access to subjects appropriate for studies of AKB-6548. As a result, the timeline for recruiting patients, conducting studies and obtaining regulatory approval of potential products may be delayed. These delays could result in increased costs, delays in advancing our development of AKB-6548 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 achieve diversity in a study, to complete our clinical studies in a timely manner. Patient enrollment is affected by factors including:

severity of the disease under investigation;
design of the study protocol;
size and nature of the patient population;
eligibility criteria for and design of the study in question;
perceived risks and benefits of the product candidate under study;
proximity and availability of clinical study sites for prospective patients;
availability of competing therapies and clinical studies and clinicians' and patients' perceptions as to the potential advantages of AKB-6548 in relation to available therapies or other products under development;
efforts to facilitate timely enrollment in clinical studies;
patient referral practices of physicians; and
ability to monitor patients adequately during and after treatment.

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

We may not be able to obtain regulatory approval in some jurisdictions outside of the United States.

We currently expect to seek regulatory approval of AKB-6548 for the treatment of anemia secondary to CKD in major markets outside the United States, including the European Union. Our ability to successfully initiate, enroll and complete a clinical study in any country outside of the United States, should we attempt to do so, is subject to numerous risks unique to conducting business in international markets, including:

difficulty in establishing or managing relationships with qualified CROs, physicians and clinical trial sites;
different local standards for the conduct of clinical studies;

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; and
the acceptability of using data obtained from studies conducted in the United States with the EMA and other regulatory authorities outside of the United States.

If we fail to successfully meet requirements for the conduct of clinical trials outside of the United States, we may be delayed in obtaining, or be unable to obtain, regulatory approval for AKB-6548 in countries outside of the United States.

Regulatory authorities outside of the United States will require compliance with numerous and varying regulatory requirements. The approval procedures vary among jurisdictions and may involve requirements for additional testing, and the time required to obtain approval may differ from that required to obtain FDA approval. In addition, in many countries outside the United States, a drug product must be approved for reimbursement before it can be approved for sale in that country. In some cases, the price that we intend to charge for our drug product is also subject to approval. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside of the United States does not ensure approval by regulatory authorities in other countries or by the FDA. However, the failure to obtain approval in one jurisdiction may negatively impact our ability to obtain approval in another jurisdiction. The regulatory approval process in countries outside of the United States may include all of the risks associated with obtaining FDA approval. We may not obtain such regulatory approvals on a timely basis, if at all. We may not be able to file for regulatory approvals and may not receive the necessary approvals to commercialize our product candidates in any market.

Clinical drug development is a lengthy and expensive process with an uncertain outcome, and positive results from the clinical studies of AKB-6548 thus far are not necessarily predictive of the results of any future clinical trials of AKB-6548. If we cannot replicate the positive results observed to date in our Phase 3 clinical trials, we may be unable to successfully develop, obtain regulatory approval for and commercialize AKB-6548.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. Success in preclinical studies may not be predictive of similar results in humans during clinical trials, and successful results from early or small clinical trials may not be replicated in later and larger clinical trials. For example, our encouraging preclinical and clinical results for AKB-6548 thus far do not ensure that the results of any future clinical trials will demonstrate similar results. Our planned Phase 3 development program will enroll a larger number of subjects and will treat subjects for longer periods than our prior trials, which will result in a greater likelihood that adverse events may be observed. Many companies in the pharmaceutical and biotechnology industries 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 AKB-6548 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 AKB-6548.

We may experience delays in our ongoing Phase 2 clinical development for AKB-6548 for the treatment of anemia in patients undergoing dialysis and we do not know whether any of our planned clinical trials will begin on time, need to be redesigned, enroll patients on time or be completed on schedule, if at all.

Clinical trials can be delayed or aborted for a variety of reasons, including delay or failure to:

obtain regulatory approval to commence a clinical trial;
reach agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
obtain institutional review board, or IRB, approval at each site;

recruit, enroll and retain patients through the completion of clinical trials;
maintain clinical sites in compliance with trial protocols through the completion of clinical trials;
address any patient safety concerns that arise during the course of the trial;
initiate or add a sufficient number of clinical trial sites; or
manufacture sufficient quantities of our product candidate for use in clinical trials.

We could encounter delays if a clinical trial is suspended or terminated by us, by the relevant IRBs at the sites at which such trials are being conducted, by the Data Safety Monitoring Board, or DSMB, for such trial or by the FDA or other regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations, clinical trial site or

manufacturing facility by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, changes in laws or regulations, or lack of adequate funding to continue the clinical trial. Any delays in completing our clinical trials will increase our costs, slow down our product candidate development and approval process and jeopardize our ability to commence product sales and generate revenue. Any of these occurrences may harm our business, financial condition and prospects significantly.

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

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

Post-approval discovery of previously unknown problems with an approved drug product, including adverse events of unanticipated severity or frequency or relating to manufacturing operations or processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of the drug product, withdrawal of the drug product from the market, or drug product recalls;
- fines, warning letters or clinical holds;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products;
- a Risk Evaluation and Mitigation Strategy (REMS) program; and
- injunctions or the imposition of civil or criminal penalties.

The FDA’s policies may change and additional government regulations may be enacted. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or are not able to maintain regulatory compliance, we may lose any marketing approval that may have been obtained and we may not achieve or sustain profitability, which would adversely affect our business.

Risks Related to our Reliance on Third Parties

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

We rely on third-party CROs and other third parties to assist in managing, monitoring and otherwise carrying out our ongoing Phase 2 development of AKB-6548 for the treatment of anemia in patients undergoing dialysis. We expect to continue to rely on third parties, such as CROs, clinical data management organizations, medical institutions and clinical investigators to conduct our clinical trials in the future, including our Phase 3 development program for

AKB-6548. We compete with many other companies for the resources of these third parties. The third parties on whom we rely may terminate their engagements with us, and having to enter into alternative arrangements would delay development and commercialization of our product candidates.

Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, the FDA and equivalent regulatory authorities outside of the United States require compliance with regulations and standards, including GCP requirements, for designing, conducting, monitoring, recording, analyzing and reporting the results of clinical trials to ensure that the data and results are credible and accurate and that the rights, integrity and confidentiality of study subjects are protected. Although we rely on third parties to conduct our clinical trials, we are responsible for ensuring that each of these clinical trials is conducted in accordance with its general investigational plan and protocol in compliance with legal and regulatory requirements. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs or clinical trial sites fail to comply with applicable GCP

requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, EMA or other regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP requirements. In addition, our clinical trials must be conducted with product that meets certain specifications and is manufactured under applicable cGMP regulations. Failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

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

We also expect to rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our products, resulting in additional losses and depriving us of potential product revenue.

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

We do not have any manufacturing facilities and do not expect to independently manufacture our product candidates for research and preclinical and clinical testing. We currently rely, and expect to continue to rely, on third parties to manufacture and supply drug product for our AKB-6548 clinical trials, and we expect to rely on third parties for the manufacture of clinical and commercial quantities of our product candidates. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

Also, these third parties may terminate their engagement with us. We believe we have sufficient drug product to complete our ongoing Phase 2 study of AKB-6548. On February 28, 2014, we entered into an agreement with Evonik Corporation, or Evonik, for the manufacture of the drug substance for the Phase 3 development program of AKB-6548. If Evonik cannot perform as agreed or terminates their engagement with us, we may be required to find replacement manufacturers. We may incur significant delays and added costs in identifying, qualifying and contracting with any such replacement, as well as producing the drug substance. Also, if we choose to engage a second source for the production of drug substance, we may incur addition costs. We also have arrangements in place for the manufacture of finished drug product for the Phase 3 development program. Although we believe that there are several other manufacturers who also could manufacture our drug product if our current drug product manufacturer cannot perform as agreed or terminates their engagement with us, we may incur significant delays and added costs in identifying, qualifying, and contracting with another manufacturer. In addition, we have to enter into technical transfer agreements and share our know-how with such third-party manufacturers, which can be time-consuming and may result in delays. These delays could result in a suspension of our clinical trials or, if AKB-6548 is approved and marketed, a failure to satisfy patient demand.

Reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured the product candidates ourselves, including:

the inability to negotiate manufacturing agreements with third parties under commercially reasonable terms;

reduced control as a result of using third-party manufacturers for all aspects of manufacturing activities, including regulatory compliance and quality assurance;
termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us;
the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
disruptions to the operations of our manufacturers or suppliers caused by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier or a catastrophic event affecting our manufacturers or suppliers.

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

The facilities used by our contract manufacturers to manufacture our product candidates must be approved by the FDA pursuant to inspections that will be conducted prior to or after we submit our NDA to the FDA. We do not control the manufacturing process of, and are completely dependent on, our contract manufacturers for compliance with cGMP requirements for manufacture of both drug substance and finished drug product. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA, we will not be able to secure and/or maintain regulatory approval for our product candidates. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA, EMA or other regulatory authorities do not approve these facilities for the manufacture of our product candidates or if they withdraw any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved. Moreover, our failure, or 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, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect the supply of our products or product candidates.

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

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

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

Completion of our clinical trials and commercialization of our product candidates require access to facilities to manufacture our product candidates at sufficient yields and at clinical and commercial scale. We have limited experience manufacturing, or managing third parties in manufacturing, any of our product candidates in the volumes that will be necessary to support large-scale clinical trials or commercial sales. Efforts to establish these capabilities may not meet initial expectations as to scheduling, scale-up, reproducibility, yield, purity, cost, potency or quality.

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

difficulties with production costs, scale-up and yields;
availability of raw materials and supplies;
quality control and assurance;
capacity constraints;
shortages of qualified personnel;
compliance with strictly enforced federal, state and international regulations that vary in each country where a product might be sold; and

lack of capital funding.

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

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

We plan to commercialize AKB-6548 ourselves in the United States and will likely seek one or more strategic collaborators to commercialize AKB-6548 in additional markets. We face competition in seeking appropriate collaborators for our product candidates, and the negotiation process is time-consuming and complex. In order for us to successfully collaborate with a third party on our product candidates, potential collaborators must view these product candidates as economically valuable. Even if we are successful in

our efforts to establish strategic collaborations, the terms that we agree upon may not be favorable to us, and we may not be able to maintain such strategic collaborations if, for example, development or approval of a product is delayed or sales of an approved product are disappointing. Any delay in entering into strategic collaboration agreements related to our product candidates could delay the development and commercialization of our product candidates and reduce their competitiveness even if they reach the market.

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

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

Risks Related to our Intellectual Property

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

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

In July 2011, a third party filed an opposition to one of our issued European patents, European Patent No. 2044005, or the ’005 Patent. During the oral proceedings, which took place on April 10, 2013, the Opposition Division of the European Patent Office decided to maintain certain claims of the patent directed to a compound chosen from a group of eight compounds, including AKB-6548, as well as claims to compositions and methods for treating various diseases including, but not limited to, anemia. Both parties have appealed the decision of the Opposition Division and final resolution of the opposition proceeding will likely take a number of years. We cannot be assured of the breadth of the claims that will remain in the ’005 Patent or that the patent will not be revoked in its entirety. If the European Patent Office decides to narrow the scope of the claims or revoke the ’005 Patent, we may not be able to establish a competitive advantage in the European Union in our market or successfully commercialize our product candidates in the European Union, which could materially adversely affect our business, operating results and financial condition.

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

The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be uncertain. The patent applications that we own or license may fail to result in issued patents in the United States or in other countries. Our competitors have and will continue to undertake formal efforts to oppose the issuance of claims in our patent applications. We do not control decisions made by the US PTO or equivalent bodies outside the United States. Even if our patents do successfully issue, third parties may challenge the validity, enforceability, inventorship, or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property or prevent others from designing around our claims. If the breadth or strength of protection provided by the patent applications we hold with respect to our product candidates is threatened, it could dissuade companies from collaborating with us to develop, and threaten our ability to commercialize, our product candidates. Further, if we encounter delays in our clinical trials, the period of time during which we could market our product candidates under patent protection would be reduced. Since patent applications in the United States and most other countries are confidential for a period of time after filing, we cannot be certain that we were the first to file any patent application related to our product candidates. Furthermore, for applications in which all claims are entitled to a priority date before March 16, 2013, an interference proceeding can be provoked by a third-party or instituted by the US PTO, to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. For applications containing a claim not entitled to priority before March 16, 2013, there is greater level of uncertainty in the patent law

with the passage of the America Invents Act (2011), which brings into effect significant changes to the U.S. patent laws and which introduces new procedures for challenging pending patent applications and issued patents. A primary change under this reform is creating a “first to file” system in the United States. This will require us to be cognizant of the time from invention to filing of a patent application.

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

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

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

In addition, these agreements typically restrict the ability of our advisors, employees, third-party contractors and consultants to publish data potentially relating to our trade secrets, although our agreements may contain certain limited publication rights. For example, any academic institution that we may collaborate with will usually expect to be granted rights to publish data arising out of such collaboration, 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, in addition to the opportunity to remove confidential or trade secret information from any such publication. In the future we may also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development or similar agreements. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of our agreements with third parties, independent development or publication of information by any of our third-party collaborators. A competitor’s discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

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

Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of third parties. The pharmaceutical and biotechnology industries are characterized by extensive litigation over patent and other intellectual property rights. We may become a party to, or 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. 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.

In addition, we are aware of subsequent U.S. patents issued to FibroGen directed to purportedly new methods of using such previously known heterocyclic carboxamide compounds for purposes of treating or affecting specified conditions. We do not believe these currently issued FibroGen U.S. patents conflict with our intellectual property rights; nor do we make any admission that any of such patents are valid or enforceable. Under U.S. law, a party may be able to patent a discovery of a new way to use a previously known compound, even if such compound itself is patented, provided the newly discovered use is novel and nonobvious. Such a method-of-use patent, however, if valid, only protects the use of a claimed compound for the specified methods claimed in the patent. This type of patent does not prevent persons from using the compound for any previously known use of the compound. Further, this type of patent does not prevent persons from making and marketing the compound for an indication that is outside the scope of the patented method. We are not aware of any valid U.S. patents issued to FibroGen, or any other person, that claim methods of using any of our product candidates for purposes of inhibiting hypoxia-inducible factor prolyl hydroxylases, or HIF-PHs, for the treatment of anemia secondary to CKD. In June 2013, the European Patent Office granted European Patent No. 1463823, or the ’823 patent, to FibroGen. The ’823 patent claims, among other things, the use of a heterocyclic carboxamide compound selected from the group consisting of pyridine carboxamides, quinoline carboxamides, isoquinoline carboxamides, cinnoline carboxamides, and beta-carboline carboxamides that inhibits HIF-PH enzyme activity in the manufacture of a medicament for increasing endogenous EPO in the prevention, pretreatment or treatment of anemia. On December 5, 2013, we filed an opposition to the ’823 patent requesting that the ’823 patent be revoked in its entirety. While, for the reasons set forth in our opposition, we believe the ’823 patent should be revoked in its entirety, the ultimate outcome of the opposition remains uncertain. If the European Patent Office decides not to revoke the ’823 patent in its entirety, or only certain claims of the ’823 patent, and any surviving claims are determined to encompass our intended use of our lead product candidate, we may not be able to commercialize our lead product candidate in the European Union for its intended use, which could materially adversely affect our business, operating results and financial condition.

FibroGen has filed patent applications related to the ’823 patent in the United States and in other countries, and some of these applications have since issued as patents outside of the U.S., such as Japanese Patent No. 4804131, or the ’131 patent. On June 2, 2014, we filed an invalidity proceeding in the Japanese Patent Office challenging the validity of the ’131 patent and requesting that it be revoked in its entirety. An oral hearing before the Japanese Patent Office was held on February 9, 2015. While, for the reasons set forth in our Request For Trial and subsequent briefing filed in that proceeding, we believe the ’131 patent should be revoked in its entirety, the ultimate outcome of the invalidity proceeding remains uncertain. If the Japanese Patent Office decides not to revoke the ’131 patent in its entirety, or only certain claims of the ’131 patent, and any surviving claims are determined to encompass our intended use of our lead product candidate, we may not be able to commercialize our lead product candidate in Japan for its intended use, which could materially adversely affect our business, operating results and financial condition. FibroGen is also pursuing other patent applications in the United States and other countries, and some of these have 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 those patents.

There may be patents of third parties, including FibroGen, of which we are currently unaware with claims to 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 these patents or

others and may challenge our ability to commercialize AKB-6548.

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 AKB-6548 or AKB-6899. 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.

We are currently involved in two opposition proceedings in the European Patent Office and one invalidity proceeding in the Japanese Patent Office. These proceedings may be ongoing for a number of years and may involve substantial expense and diversion of employee resources from our business. In addition, we may become involved in additional opposition proceedings or other legal or administrative proceedings in the future. For more information, see the other risk factors under "Risks Related to Intellectual Property."

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.

Various administrative proceedings are also available for challenging patents, including interference, reexamination, inter partes review, and post-grant review proceedings before the US PTO or oppositions and other comparable proceedings in foreign jurisdictions. Interference proceedings provoked by third parties or brought by the US PTO may be necessary to determine the priority of inventions with respect to our patents or patent applications. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms or at all. Even if we are successful, participation in interference or other administrative proceedings before the US PTO or a foreign patent office may result in substantial costs and distract our management and other employees.

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

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

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

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

We have received confidential and proprietary information from collaborators, prospective licensees and other third parties. In addition, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies. We may be

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

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

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

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

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 AKB-6548, AKB-6899 or any other product candidates that we may develop or acquire in the future, these product candidates may not gain market acceptance among physicians, third-party payors, patients and others in the medical community. In addition, market acceptance of any approved products depends on a number of other factors, including:

the efficacy and safety of the product, as demonstrated in clinical trials;
the clinical indications for which the product is approved and the product label approved by regulatory authorities, including any warnings that may be required on the label;

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 availability of adequate coverage and reimbursement by third-party payors and government authorities;
the ability to contract with dialysis providers;
relative convenience and ease of administration;
the prevalence and severity of adverse side effects;
the effectiveness of our sales and marketing efforts; and
the restrictions on the use of our products together with other medications, if any.

For example, two of the largest operators of dialysis clinics in the United States, DaVita, Inc., or DaVita, and Fresenius Medical Care, or Fresenius, account for more than half of the injectable rESA sales in the U.S. dialysis market and have entered into long-term

supply agreements with Amgen Inc., or Amgen, that began in January 2012. We believe that it may be challenging to enter into long or short-term supply agreements with DaVita, Fresenius or other operators of dialysis clinics.

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

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

We do not have a sales or marketing infrastructure and we have not yet sold, marketed or distributed any of our products. To achieve commercial success for any product for which we obtain marketing approval, we will need to establish a sales and marketing organization or make arrangements with third parties to perform these services.

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

Factors that may inhibit our efforts to commercialize our products on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to and educate physicians regarding our products;
- our inability to effectively manage a geographically dispersed sales and marketing team;
- the 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
- unforeseen costs and expenses associated with creating a sales and marketing organization.

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

Coverage and reimbursement may be limited or unavailable in certain market segments for any approved products, 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 pay for and establish formularies and 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;
cost-effective; and
neither experimental nor investigational.

Obtaining coverage and reimbursement approval for a product from a government or other third-party payor is a time consuming and costly process that could require us to provide supporting scientific, clinical and cost-effectiveness data for the use of our products to the payor. Additionally, we may be required to enter into contracts with third-party payors to obtain favorable formulary status. We

may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement. We cannot be sure that coverage or adequate reimbursement will be available for any of our product candidates. Even if we obtain coverage for our product candidates, third-party payors may not establish adequate reimbursement amounts, which may reduce the demand for, or the price of, our products. If reimbursement is not available or limited, we may not be able to commercialize certain of our products. In addition, in the United States third-party payors are increasingly attempting to contain healthcare costs by limiting both coverage and the level of reimbursement of new drugs. As a result, significant uncertainty exists as to whether and how much third-party payors will provide reimbursement for newly approved drugs, which in turn will put pressure on the pricing of drugs.

In addition, if AKB-6548 is used in an outpatient dialysis facility, such facilities often receive fixed reimbursement for all dialysis services furnished to patients with end-stage renal disease, or ESRD. For example, Medicare payments to ESRD facilities for such services are based on a prospective payment system known as the basic case-mix adjusted composite payment system. These payments cover a bundle of items and services routinely required for dialysis treatments furnished to Medicare beneficiaries in Medicare-certified ESRD facilities or at their home, including the cost of certain routine drugs such as our product candidates. Patient and provider access to adequate coverage and reimbursement by government and private insurance plans is central to the acceptance of any products for which we receive regulatory approval. We may be unable to sell AKB-6548, if approved, to dialysis providers on a profitable basis if third-party payors reduce their current levels of payment or if our costs of production increase faster than increases in reimbursement levels.

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

In some countries, particularly member states of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after receipt of marketing approval for a product. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. In some countries, we may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our product candidates to other available products in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third-party payors or government authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be adversely affected.

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

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

In the United States, the Medicare Prescription Drug, Improvement and Modernization Act of 2003, also called the MMA, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for physician-administered drugs. In addition, this legislation provided authority for limiting the number of

drugs that will be covered in any therapeutic class. As a result of this legislation and the expansion of federal coverage of drug products, we expect that there will be additional pressure to reduce costs. For example, the Centers for Medicare and Medicaid Services, or CMS, has enacted regulations that reduced capitated payments to dialysis providers. These cost reduction initiatives and other provisions of this legislation could decrease the scope of coverage and the price that we receive for any approved products and could seriously harm our business. While the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policies and payment limitations in setting their own reimbursement rates, and any reduction in reimbursement that results from the MMA may cause a similar reduction in payments from private payors. Similar regulations or reimbursement policies may be enacted in international markets which could similarly impact our business.

In addition, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively PPACA, was enacted in 2010 with a goal of reducing the cost of healthcare and substantially changing the way healthcare is financed by both government and private insurers. The PPACA, among other things, increases the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extends the rebate program to individuals enrolled in Medicaid managed care organizations, establishes annual fees and taxes on manufacturers of certain branded prescription drugs, and creates a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the

manufacturer's outpatient drugs to be covered under Medicare Part D. In addition, other legislative changes have been proposed and adopted in the United States since the PPACA was enacted. On August 2, 2011, the Budget Control Act of 2011 created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of up to 2% per fiscal year, which went into effect on April 1, 2013.

It is likely that federal and state legislatures within the United States and governments in other countries 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 drug products for which we may obtain regulatory approval;
our ability to set a price that we believe is fair for our products;
our ability to obtain coverage and reimbursement approval for a product;
our ability to generate revenue and achieve or maintain profitability; and
the level of taxes that we are required to pay.

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

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

the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, the purchase or recommendation of an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;
federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent;
the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;
HIPAA, as amended by the Health Information Technology and Clinical Health Act, or HITECH, and its implementing regulations, which imposes certain requirements relating to the privacy, security, and transmission of individually identifiable health information;
the federal physician "sunshine" requirements under PPACA, which requires manufacturers of drugs, devices, biologics, and medical supplies to report annually to CMS information related to payments and other transfers of value to physicians, other healthcare providers, and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members;
state law equivalents of each of the above 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; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government, or otherwise restrict payments that may be

made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways, thus complicating compliance efforts.

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

of the False Claims Act. To constitute a false claim prior to this amendment, an anti-kickback violation had to be accompanied by a false statement, such as false certification of compliance.

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 penalties, including civil and criminal penalties, damages, fines, the curtailment or restructuring of our operations, the exclusion from participation in federal and state healthcare programs and imprisonment, any of which could materially adversely affect our ability to operate our business and our financial results.

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

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

If AKB-6548 is approved and launched commercially, competing drugs may include EPOGEN® and Aranesp®, commercialized by Amgen, Procrit® and Eprex®, commercialized by Johnson & Johnson, and Mircera®, commercialized by Roche Holding Ltd., or Roche. We may face competition from potential new anemia therapies. There are several other HIF product candidates in various stages of active development for anemia indications that may be in direct competition with AKB-6548 if and when they are approved and launched commercially. These candidates are being developed by such companies as FibroGen, in partnership 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/Astellas Pharma Inc., in particular, is currently in Phase 3 clinical development of its product candidate, FG-4592 (roxadustat). Some of these product candidates may enter the market as early as 2017. In addition, certain companies are developing potential new therapies for renal-related diseases that could potentially reduce rESA utilization and thus limit the market for AKB-6548 if and when it is approved and launched commercially. Other new therapies are in development for the treatment of conditions inclusive of renal anemia, like sotatercept® from Acceleron Pharma Inc, that may impact the market for anemia-targeted treatment.

Since rESAs are biologic products, the introduction of biosimilars into the rESA market in the United States will constitute additional competition for AKB-6548 if we are able to obtain approval for and commercially launch our product. A biosimilar product is a follow-on version of an existing, branded biologic product. The patents for the existing, branded product must expire in a given market before biosimilars may enter that market without risk of being sued for patent infringement. In addition, an application for a biosimilar product cannot be approved by the FDA until 12 years after the existing, branded product was approved under a Biologics License Application, or BLA. The patents for epoetin alfa, an rESA, expired in 2004 in the European Union, and the remaining patents have expired or will expire between 2012 and 2015 in the United States. Several biosimilar versions of rESAs are available for sale in the European Union and biosimilar versions of rESAs are currently being studied in clinical trials in the United States.

Many of our potential competitors have significantly greater financial, manufacturing, marketing, drug development, technical and human resources than we do. Large pharmaceutical companies, in particular, have extensive experience in clinical testing, obtaining regulatory approvals, recruiting patients and manufacturing pharmaceutical products. Large and established companies such as Amgen and Roche, among others, compete in the market for drug products to treat anemia. In particular, these companies have greater experience and expertise in securing government contracts and grants to support their research and development efforts, conducting pre-clinical testing and clinical trials, obtaining regulatory approvals to market products, manufacturing such products on a broad scale and marketing

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

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

Undesirable side effects caused by our products or even competing products in development that utilize a common mechanism of action could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in the denial of regulatory approval by the FDA or other regulatory authorities and potential product liability claims. We recently completed a Phase 2b study of

AKB-6548 in non-dialysis patients with anemia related to CKD. The incidence of the most common treatment emergent adverse events in the Phase 2b study were well balanced overall between the AKB-6548 and placebo treatment groups. There was a higher incidence of serious adverse events (SAEs) reported in the AKB-6548 treatment group, the most common being renal-related. Serious adverse events deemed to be possibly or probably related to AKB-6548 could have a material adverse effect on the development of our product candidates and our business as a whole. Our understanding of adverse events in future clinical trials of other 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, or enrolled patients may not want to complete a clinical trial;
we may be unable to obtain regulatory approval for our product candidates or regulatory authorities may withdraw approvals of product candidates;
regulatory authorities may require additional warnings on the label;
a medication guide outlining the risks of such side effects for distribution to patients may be required;
we could be sued and held liable for harm caused to patients; and
our reputation may suffer.

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

Risks Related to our Business and Industry

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

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be critical to our success. We are highly dependent on certain members of our senior management. The loss of the services of our executive officers 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 executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products. We may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the intense competition among numerous biopharmaceutical companies for similar personnel.

In addition, certain of our current employees also provide services to Aerpio Therapeutics, Inc., or Aerpio, a company we spun out in 2011, under a services agreement between Akebia and Aerpio. As a result, these employees devote some of their time to activities relating to Aerpio’s business. In addition, some of our employees who provide services to Aerpio may ultimately become full-time employees of Aerpio and we will be forced to hire additional personnel to replace them.

We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

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

We are exposed to the risk that our employees, independent contractors, principal investigators, CROs, consultants and vendors may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or unauthorized activities that violate (1) FDA regulations, including those laws that require the reporting of true, complete and accurate information to the FDA, (2) quality standards, including Good Laboratory Practices (GLP), Good Clinical Practices (GCP) and Good Manufacturing Practices (GMP) (3) federal and state healthcare fraud and abuse laws and regulations or (4) laws that require the reporting of true and accurate financial information and data or (5) securities laws and regulations. Specifically, sales,

marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. It is not always possible to identify and deter misconduct by employees and third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, 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, and curtailment of our operations, 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 development, regulatory, manufacturing, marketing and sales capabilities or contract with third parties to provide these capabilities for us. As our operations expand, we expect that we will need to manage additional relationships with various strategic collaborators, suppliers and other third parties. Future growth will impose significant added responsibilities on members of management. Our future financial performance and our ability to commercialize AKB-6548, 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 and integrate additional personnel. We may not be able to accomplish these tasks, and our failure to accomplish any of them could prevent us from successfully growing our company.

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

We face an inherent risk of product liability as a result of the clinical testing of our product candidates and will face an even greater risk if we commercialize any products. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability and breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Even a successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, 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 covering our clinical trials in the amount of $10 million in the aggregate. Although we maintain product liability insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts.

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

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

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

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

We may not be able to win government, academic institution or non-profit contracts or grants.

From time to time, we may apply for contracts or grants from government agencies, non-profit entities and academic institutions. Such contracts or grants can be highly attractive because they provide capital to fund the on-going development of our product candidates without diluting our stockholders. However, there is often significant competition for these contracts or grants. Entities offering contracts or grants may have eligibility requirements that our competitors may be able to satisfy that we cannot. In addition, such entities may make arbitrary decisions as to whether to offer contracts or make grants, to whom the contracts or grants will be awarded and the size of the contracts or grants to each grantee. Even if we are able to satisfy the award requirements, there is no guarantee that we will be awarded the grant. Therefore, we may not be able to win any contracts or grants in a timely manner, if at all.

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 may 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 if the market value of our common stock held by non-affiliates exceeds $700 million as of any September 30 before that time or if we have total annual gross revenue of $1 billion or more during any fiscal year before that time, in which cases we would no longer be an emerging growth company as of the following December 31 or, 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 IPO in March 2014, the price of our common stock as reported on The NASDAQ Global Market has ranged from a low of $8.47 on February 13, 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, including the risks described in Item 1A.

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

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

Our executive officers, directors and principal stockholders, together with their respective affiliates collectively control a majority of our common stock. Accordingly, these stockholders will be able to exert a significant degree of influence over our management and affairs and over matters requiring stockholder approval, including the election of our Board of Directors and approval of significant corporate transactions. This concentration of ownership could have the effect of entrenching our management and/or the Board of Directors, delaying or preventing a change in our control or otherwise discouraging a potential acquirer from attempting to obtain control of us, which in turn could have a material and adverse effect on the fair market value of our common stock.

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

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

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

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

authorize “blank check” preferred stock, which could be issued by our Board of Directors without stockholder approval and may contain voting, liquidation, dividend and other rights superior to our common stock;
create a classified Board of Directors whose members serve staggered three-year terms;
specify that special meetings of our stockholders can be called only by our Board of Directors pursuant to a resolution adopted by a majority of the total number of directors;

prohibit stockholder action by written consent;
establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our Board of Directors;
provide that our directors may be removed only for cause;
provide that vacancies on our Board of Directors may be filled only by a majority of directors then in office, even though less than a quorum;
require a supermajority vote of the holders of our common stock or the majority vote of our Board of Directors to amend our Amended and Restated By-Laws; and
require a supermajority vote of the holders of our common stock to amend the classification of our Board of Directors into three classes and to amend certain other provisions of our Amended and Restated Certificate of Incorporation.

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

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

Any provision of our Amended and Restated Certificate of Incorporation, our Amended and Restated By-Laws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock.

Our ability to use net operating losses to offset future taxable income may be subject to certain limitations.

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

Our Amended and Restated Certificate of Incorporation designates the state or federal courts located in the State of Delaware as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders’ ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our Amended and Restated Certificate of Incorporation provides that, subject to limited exceptions, the state and federal courts located in the State of Delaware will be the sole and exclusive forum for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, (3) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law, our Amended and Restated Certificate of

Incorporation or our Amended and Restated By-Laws or (4) any other action asserting a claim against us that is governed by the internal affairs doctrine. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our Amended and Restated Certificate of Incorporation described above. This choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and employees. Alternatively, if a court were to find these provisions of our Amended and Restated Certificate of Incorporation inapplicable to, or unenforceable with respect to, one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions, which could adversely affect our business and financial condition.

Item 1B. Unresolved Staff Comments
None

Item 2. Properties
Our corporate headquarters are located in Cambridge, Massachusetts. We currently lease approximately 15,367 square feet of office space in Cambridge, Massachusetts under a lease that expires on December 31, 2016. 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
In July 2011, a third party filed an opposition to our issued European Patent No. 2044005, or the ’005 Patent. During the oral proceedings, which took place on April 10, 2013, the Opposition Division of the European Patent Office maintained the ’005 Patent on the basis of the third auxiliary request filed during the oral proceedings. This decision resulted in the maintenance of a claim directed to a compound chosen from a group of eight compounds, including AKB-6548, as well as claims to compositions and methods for treating various diseases, including, but not limited to, anemia. Both parties have appealed the decision of the Opposition Division and final resolution of the opposition proceedings will likely take a number of years. We cannot be assured of the breadth of the claims that will remain in the ’005 Patent or that the patent will not be revoked in its entirety.

In June 2013, the European Patent Office granted European Patent No. 1463823, or the ’823 patent, to FibroGen, Inc., or FibroGen. The ’823 patent claims, among other things, the use of a heterocyclic carboxamide compound selected from the group consisting of pyridine carboxamides, quinoline carboxamides, isoquinoline carboxamides, cinnoline carboxamides, and beta-carboline carboxamides that inhibits HIF-PH enzyme activity in the manufacture of a medicament for increasing endogenous EPO in the prevention, pretreatment or treatment of anemia. On December 5, 2013, we filed an opposition to the ’823 patent requesting that the ’823 patent be revoked in its entirety. While, for the reasons set forth in our opposition, we believe the ’823 patent should be revoked in its entirety, the ultimate outcome of the opposition remains uncertain. If the European Patent Office decides not to revoke the ’823 patent in its entirety, or only certain claims of the ’823 patent, and any surviving claims are determined to encompass our intended use of our lead product candidate, we may not be able to commercialize our lead product candidate in the European Union for its intended use, which could materially adversely affect our business, operating results and financial condition.

In August 2011, the Japanese Patent Office granted Japanese Patent No. 4804131, or the ’131 patent, to FibroGen. The ’131 patent claims, among other things, the use of certain heterocyclic carboxamides selected from the group consisting of pyridine carboxamides, quinoline carboxamides, and isoquinoline carboxamides to treat anemia, wherein the heterocyclic carboxamides also suppress HIF prolyl hydroxylase. On June 2, 2014, we filed an invalidity proceeding in the Japanese Patent Office challenging the validity of the ’131 patent and requesting that it be revoked in its entirety. An oral hearing before the Japanese Patent Office was held on February 9, 2015. While, for the reasons set forth in our Request For Trial and subsequent briefing filed in that proceeding, we believe the ’131 patent should be revoked in its entirety, the ultimate outcome of the invalidity proceeding remains uncertain. If the Japanese Patent Office decides not to revoke the ’131 patent in its entirety, or only certain claims of the ’131 patent, and any surviving claims are determined to encompass our intended use of our lead product candidate, we may not be able to commercialize our lead product candidate in Japan for its intended use, which could materially adversely affect our business, operating results and financial condition.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

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

Market Price Information

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

	High	Low
2014		
First Quarter from and after March 20th	$28.50	$18.75
Second Quarter	$31.00	$16.41
Third Quarter	$28.33	$20.10
Fourth Quarter	$21.75	$8.60

Holders

At February 17, 2015, there were approximately 44 holders of record of our common stock. We believe that the number of beneficial owners of our common stock at that date was substantially greater.

Dividends

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

Recent Sales of Unregistered Securities

Between January 1, 2014 and December 31, 2014, we issued and sold an aggregate of 116,394 shares of common stock to certain employee for cash consideration in the aggregate amount of $88,838 upon the exercise of stock options. These issuances were undertaken in reliance upon the exemption from registration requirements of Rule 701 of the Securities Act.

Issuer Purchases of Equity Securities

The following table contains information regarding purchases of our common stock made during the quarter ended December 31, 2014 by or on behalf of Akebia Therapeutics, Inc. or any "affiliated purchasers," as defined by Rule 10b-18(a)(3) of the Securities Exchange Act of 1934:

Period	Total Number of Share Purchased	Average Price Paid Per Share	Total Number of Shares Purchased as Part of Publicly Announced Plans or Programs	Approximate Dollar Value of Share that May Yet be Purchased Under the Plans or Programs
10/01/2014 - 10/31/2104	—	$ —	—	$ —
11/10/2014 - 11/30/2014	—	—	—	—
12/01/2014 - 12/31/2014	5,910	11.43	—	—
Total	5,910	$ 11.43	—	$ —

Use of Proceeds from Initial Public Offering of Common Stock

On March 25, 2014, we completed the IPO of our common stock and issued and sold 6,762,000 shares of our common stock, including 879,647 shares of common stock sold pursuant to the underwriters' full exercise of their option to purchase additional shares at a public offering price of $17.00 per share, for aggregate gross proceeds of $115.0 million. All of the shares issued and sold in the IPO were registered under the Securities Act pursuant to a Registration Statement on Form S-1 (File No. 333-193969), which was declared effective by the SEC on March 19, 2014.

The net proceeds to us, after deducting underwriting discounts of $8.0 million and offering expenses totaling $2.5 million, were approximately $104.4 million. No offering expenses were paid directly or indirectly to any of our directors or officers (or their associates) or persons owning 10.0% or more of any class of our equity securities or to any other affiliates.

There has been no material change in our planned use of the balance of the net proceeds from the offering described in our final prospectus filed with the SEC pursuant to Rule 424(b) under the Securities Act. We invested the funds received in cash equivalents and other investments in accordance with our investment policy, and as of December 31, 2014, the remainder of the net proceeds is included in cash and cash equivalents and available for sale securities.

Comparative Stock Performance Graph

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

	3/19/2014	3/31/2014	4/30/2014	5/31/2014	6/30/2014	7/31/2014	8/31/2014	9/30/2014	10/31/2014	11/30/2014	12/31/2014
Akebia Therapeutics Inc	$100.00	$115.06	$143.35	$142.94	$163.47	$130.24	$132.41	$130.18	$76.24	$71.06	$68.47
NASDAQ Composite-Total Returns	$100.00	$97.51	$95.59	$98.74	$102.69	$101.85	$106.93	$104.99	$108.24	$112.19	$110.97
NASDAQ Biotechnology Index	$100.00	$91.04	$88.59	$92.37	$99.13	$96.81	$106.79	$105.56	$114.55	$117.44	$117.37

Equity Compensation Plan Information

We have two equity compensation plans, which have both been approved by our shareholders: the 2014 Incentive Plan and the 2014 Employee Stock Purchase Plan. Upon the conclusion of our IPO, we ceased to make grants under the 2008 Equity Incentive Plan.

The following table sets forth the number and weighted-average exercise price of ordinary shares to be issued upon exercise of outstanding options, warrants and rights, and the number of securities remaining available for future issuance under all of our equity compensation plans, at December 31, 2014.

Plan Category	Number of securities to be issued upon exercise of outstanding options, warrants and rights (a)	Weighted-average exercise price of outstanding options, warrants and rights (b)	Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a)) (c)
Equity compensation plans approved by security holders	1,526,346	$ 7.57	1,549,154
Equity compensation plans not approved by security holders	—	—	—
Total	1,526,346	$ 7.57	1,549,154

Item 6. Selected Financial Data

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

	Year Ended December 31,		
	2014	2013	2012
	(in thousands, except share and per share data)		
Consolidated statements of operations data:			
Operating expenses:			
Research and development	$25,398	$10,781	$5,632
General and administrative	12,542	5,152	2,891
Total operating expenses	37,940	15,933	8,523
Loss from operations	(37,940)	(15,933)	(8,523)
Other income, net	906	2,766	327
Net loss	$(37,034)	$(13,167)	$(8,196)
Accretion on preferred stock	(86,899)	(55,886)	(3,323)
Net loss applicable to common shareholders	$(123,933)	$(69,053)	$(11,519)
Net loss per share applicable to common stockholders—basic and diluted[1]	$(8.04)	$(126.94)	$(27.82)
Weighted-average number of common shares used in net loss per share applicable to common stockholders—basic and diluted	15,406,386	544,002	414,107

(1) See Note 12 within the notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K for a description of the method used to calculate basic and diluted net loss per share of common stock.

	December 31,		
	2014	2013	2012
	(in thousands)		
Balance Sheet Data:			
Cash and cash equivalents and available for sale securities	$108,918	$32,556	$1,641
Working capital (deficit)	103,595	29,529	(2,679)
Total assets	110,995	34,665	2,244

Redeemable convertible preferred stock	-	157,827	56,909
Accumulated deficit	(100,673)	(127,072)	(59,588)
Total stockholders' equity (deficit)	104,078	(127,072)	(59,588)

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

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

Overview

We are a biopharmaceutical company focused on delivering innovative therapies to patients with kidney disease through the biology of hypoxia-inducible factor, or HIF. HIF is the primary regulator of the production of red blood cells, or RBCs, in the body and potentially a novel mechanism of treating anemia. Our lead product candidate, AKB-6548, is being developed as a once-daily, oral therapy that has successfully completed a Phase 2b study demonstrating that AKB-6548 can safely and predictably raise hemoglobin levels in non-dialysis patients with anemia related to chronic kidney disease, or CKD.

On October 27, 2014, we announced positive top-line results from our Phase 2b study of AKB-6548 in non-dialysis patients with anemia related to CKD, and we expect complete efficacy and safety data to be presented in the first half of 2015. We expect to initiate Phase 3 studies for anemia secondary to CKD in 2015 and would anticipate submitting an NDA for AKB-6548 in the United States by 2019, if the Phase 3 data are favorable. We have also initiated Phase 2 clinical development for AKB-6548 for the treatment of anemia in patients undergoing dialysis, the second indication we will pursue. The results from that study are expected in the third quarter of 2015. We have also commenced discussions with European regulatory authorities in the first quarter of 2015, with the goal of potentially also submitting European marketing application(s). Also in the third quarter of 2014, we completed a thorough QT (TQT) study, demonstrating that AKB-6548 does not have an adverse effect on cardiac repolarization or conduction (i.e., negative TQT study).

Our preclinical candidate, AKB-6899, is a small molecule with distinctive biochemical and physiological properties that may be beneficial for treatment of certain cancers. In several preclinical mouse models, AKB-6899 has been active in reducing tumor growth and development of metastases. Therefore, Investigational New Drug, or IND, enabling studies are being performed with the goal of opening an IND with the U.S. Food and Drug Administration (FDA) in 2015.

We own global rights to our HIF-based product candidates, including AKB-6548. If approved by regulatory authorities, we plan to commercialize AKB-6548 in the United States ourselves and intend to seek one or more collaborators to commercialize the product candidate in additional markets.

Since our inception in 2007, we have devoted the largest portion of our resources to our development efforts relating to AKB-6548, including preparing for and conducting clinical studies of AKB-6548, 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 our IPO and the private placement of preferred stock, common stock and convertible notes.

In December 2011, we distributed our programs focused on the treatment of diabetic eye disease and inflammatory bowel disease into Aerpio, which has since operated as a stand-alone company. We currently have administrative services agreements with Aerpio under which we obtain from, and provide to, Aerpio certain services including consulting services and use of premises.

We have never been profitable and have incurred net losses in each year since inception. Our net losses were $37.0 million and $13.2 million for the years ended December 31, 2014 and 2013, 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:

continue our Phase 2 clinical study of AKB-6548 for the treatment of anemia in patients undergoing dialysis;
prepare for and initiate a global Phase 3 development program of AKB-6548 for the treatment of anemia secondary to CKD;
seek regulatory approvals for our product candidates that successfully complete clinical trials;

have our product candidates manufactured for clinical trials and for commercial sale;
establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval;
continue preclinical and clinical development for AKB-6899;
initiate additional preclinical, clinical or other studies for additional indications for AKB-6548, AKB 6899 and other product candidates that we may develop or acquire;
seek to discover and develop additional product candidates;
acquire or in-license other commercial products, product candidates and technologies;
make royalty, milestone or other payments under any future in-license agreements;
maintain, protect and expand our intellectual property portfolio;
attract and retain skilled personnel; and
create additional infrastructure to support our operations as a public company.

We do not expect to generate revenue from product sales unless and until we successfully complete development and obtain regulatory approval for one or more of our product candidates, which we expect will take a number of years and is subject to significant uncertainty. We have no manufacturing facilities, and all of our manufacturing activities are contracted out to third parties. Additionally, we currently utilize third-party clinical research organizations, or CROs, to carry out our clinical development activities, and we do not yet have a sales organization. If we obtain regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. Accordingly, we will seek to fund our operations through public or private equity or debt financings or other sources. However, we may be unable to raise additional funds or enter into other arrangements when needed on favorable terms or at all. Our failure to raise capital or enter into such other arrangements as and when needed would have a negative impact on our financial condition and our ability to develop our products.

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

On March 25, 2014, we completed our IPO whereby we sold 6,762,000 shares of common stock, including 879,647 shares of common stock pursuant to the full exercise of an over-allotment option granted to the underwriters, at a price of $17.00 per share. The shares began trading on the Nasdaq Global Market on March 20, 2014. The aggregate net proceeds received by us from the offering were $104,364,560, net of underwriting discounts and commissions and estimated offering expenses. Upon the closing of the IPO, all of our outstanding shares of convertible redeemable preferred stock converted into 12,115,183 shares of common stock. Additionally, we are now authorized to issue 175,000,000 shares of common stock and 25,000,000 shares of preferred stock.

Financial Operations Overview

Revenue

To date, we have not generated any revenue from the sales of products or other means. Our ability to generate product revenue and become profitable depends upon our ability to successfully develop and commercialize products. We expect to incur losses for the foreseeable future, and we expect these losses to increase as we continue our development of, and seek regulatory approvals for, our product candidates and begin to commercialize any approved products. Because of the numerous risks and uncertainties associated with product development, we are unable to

predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability. Even if we are able to generate revenue from the sale of our products, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce our operations.

Research and Development Expenses

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

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

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

We cannot determine with certainty the duration and completion costs of the current or future clinical studies of our product candidates or if, when, or to what extent we will generate revenue from the commercialization and sale of any of our product candidates that obtain regulatory approval. We may never succeed in achieving regulatory approval for any of our product candidates.

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

- the rate of progress of, results of and cost of completing our Phase 2 clinical development for AKB-6548 for the treatment of anemia in patients undergoing dialysis;
- assuming the AKB-6548 clinical development program for CKD patients not on dialysis advances to Phase 3, the scope, size, rate of progress, results and costs of initiating and completing our Phase 3 development program of AKB-6548;
- the scope, progress, results and costs of preclinical development, laboratory testing and clinical studies for AKB-6899 and any other product candidates that we may develop or acquire;
- the cost of having our product candidates manufactured for clinical trials;
- difficulties or delays in enrolling patients in our clinical trials;
- unanticipated changes to laws or regulations applicable to our clinical trials; and
- the timing of, and the costs involved in, obtaining regulatory approvals for AKB-6548 and any other product candidates, if clinical trials are successful.

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

From inception through December 31, 2014, we have incurred $77.1 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 AKB-6548 and AKB-6899. Our current and planned research and development activities include the following:

- We have completed a Phase 2b study during 2014 to examine the safety and efficacy of AKB-6548 in non-dialysis patients with anemia related to CKD, and we will prepare the data for presentation at the World Congress of Nephrology meeting in March 2015 and other scientific meetings.

We plan to initiate a Phase 3 development program for AKB-6548 in 2015 for anemia secondary to CKD in patients not on dialysis.

We have begun Phase 2 clinical development for AKB-6548 for the treatment of anemia in patients undergoing dialysis, the second indication we will pursue. The results from that study are expected in the third quarter of 2015.

We intend to file an IND and begin Phase 1 studies for AKB-6899.

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

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

General and Administrative Expenses

We obtain from, and provide to, Aerpio services under the terms of administrative services agreements between the two companies. See “Certain Relationships and Related Party Transactions.” General and administrative expenses consist primarily of salaries and related costs for personnel, including stock-based compensation and travel expenses. Other general and administrative expense 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 financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, and expenses and the disclosure of contingent assets and liabilities in our financial statements. On an ongoing basis, we evaluate our estimates and judgments, including those related to accrued expenses and stock-based compensation. We base our estimates on historical experience, known trends and events, and various other factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in the notes to our 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 financial statements.

Accrued Research and Development Expenses

As part of the process of preparing our financial statements, we are required to estimate our accrued 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 accrued expenses as of each balance sheet date in our 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 accrued research and development expenses include expenses for:

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

We base our expenses related to clinical studies on our estimates of the services received and efforts expended pursuant to contracts with multiple CROs that conduct and manage clinical studies on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. The scope of services under these contracts 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 and shares of common stock. 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 FASB 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. Following the consummation of our IPO, stock option, common stock and restricted stock values are determined based on the quoted market price of our common stock.

We estimate the fair value of our stock-based awards of options to purchase shares of common stock to employees and non-employees using the Black-Scholes option pricing model, which requires the input of highly subjective assumptions, including (a) the expected stock price volatility, (b) the calculation of the expected term of the award, (c) the risk-free interest rate and (d) expected dividends. Due to the lack of a public market for the trading of our common stock and a lack of company-specific historical and implied volatility data, we have based our estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. The historical volatility is calculated based on a period of time commensurate with the expected term assumption. The computation of expected volatility is based on the historical volatility of a representative group of companies with similar characteristics to our company, including stage of product development and life science industry focus. We are a company in a very early stage of product development with no revenue and the representative group of companies has certain similar characteristics. We believe the group selected has sufficient similar economic and industry characteristics, and includes companies that are most representative of our company. We use the simplified method as prescribed by the SEC Staff Accounting Bulletin No. 107, Share-Based Payment, to calculate the expected term for options granted to employees as we do not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. The expected term is applied to the stock option grant group as a whole, as we do not expect substantially different exercise or post-vesting termination behavior among our employee population. For options granted to non-employees, we utilize the contractual term of the arrangement as the basis for the expected term assumption. The risk-free interest rate is based on a treasury instrument whose term is consistent with the expected life of the stock options. The expected dividend yield is assumed to be zero as we have never paid dividends and have no current plans to pay any dividends on our common stock, similar to our peer group. We estimate grant date fair value of restricted stock awards with corresponding promissory notes using the Black-Scholes option pricing model. Post IPO, the grant date fair value of restricted stock award grants without a promissory note and awards of common stock has been based on the estimated value of our common stock at the date of grant.

Our stock-based awards are subject to either service or performance-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. Compensation expense related to awards to employees with performance-based vesting conditions is recognized based on the grant date fair value over the requisite service period using the accelerated attribution method to the extent achievement of the performance condition is probable. Consistent with the guidance in ASC 505-50, compensation expense related to awards to non-employees with performance-based vesting conditions is recognized based on the then-current fair value at each financial reporting date prior to the measurement date over the requisite service period using the accelerated attribution method to the extent achievement of the performance condition is probable.

We are also required to estimate forfeitures at the time of grant, and revise those estimates in subsequent periods if actual forfeitures differ from our estimates. We use historical data to estimate pre-vesting forfeitures and record stock-based compensation expense only for those awards that are expected to vest. To the extent that actual forfeitures differ from our estimates, the difference is recorded as a

cumulative adjustment in the period the estimates were revised. Stock-based compensation expense recognized in the financial statements is based on awards that are ultimately expected to vest.

In June 2011, certain of our employees purchased shares of our restricted stock in exchange for promissory notes. Although these notes were 50% recourse to the employees, we have accounted for the promissory notes as nonrecourse in their entirety since the promissory notes are not aligned with a corresponding percentage of the underlying shares. Accordingly, we have accounted for the combination of the promissory note and restricted stock as a grant of an option, as the substance is similar to the grant of an option. The exercise price of this stock option is the principal and interest due on the promissory note. The fair value of the stock option is recognized over the requisite service period (not the term of the promissory note) through a charge to compensation cost. The maturity date of the promissory notes reflects the legal term of the stock option for purposes of valuing the award. The outstanding principal and interest on the promissory notes was paid in full during the third quarter of 2014.

Stock-based compensation totaled approximately $6.0 million and $1.6 million for the year ended December 31, 2014 and 2013, respectively.

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

Emerging Growth Company Status

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

Results of Operations

Comparison of the Years Ended December 31, 2014 and 2013

	Year ended December 31,		Increase (Decrease)
	2014	2013	
	(In Thousands)		
Operating expenses:			
Research and development	$25,398	$10,781	$ 14,617
General and administrative	12,542	5,152	7,390
Total operating expenses	37,940	15,933	22,007
Loss from operations	(37,940)	(15,933)	22,007
Other income (expense), net	906	2,766	(1,860)
Net loss	$(37,034)	$(13,167)	$ 23,867

Research and Development Expenses. Research and development expenses were $25.4 million for the year ended December 31, 2014, compared to $10.8 million for the year ended December 31, 2013. The increase of $14.6 million was primarily due to the following expense increases related to AKB-6548: Phase 2b study costs of approximately

$1.7 million due to ongoing enrollment through April 2014, $2.9 million related to the initiation and conduct of Phase 2 clinical development for the treatment of anemia in patients undergoing dialysis, $0.3 million related to Phase 3 program costs and $3.3 million related to a thorough QT (TQT) study and other clinical, non-clinical and manufacturing costs. Research and development expenses were further increased by $0.7 million of patent costs, $2.7 million of stock compensation costs, $2.5 million related to increased headcount, travel and consulting costs, and $0.3 million related to drug development for AKB-6899.

General and Administrative Expenses. General and administrative expenses were $12.5 million for the year ended December 31, 2014, compared to $5.2 million for the year ended December 31, 2013. The increase of $7.4 million was primarily due to the following expense increases: $1.8 million of stock-based compensation, $0.7 million of professional fees, $2.8 million related to increased headcount, severance and consulting costs, $1.3 million related to insurance and facilities and $0.7 million in commercial planning costs.

Other Income (Expense), Net. Other income (expense), net, was $0.9 million for the year ended December 31, 2014, compared to $2.8 million for the year ended December 31, 2013. Other income (expense), net for the year ended December 31, 2014, is primarily related to reimbursements from Aerpio for employee-related costs of approximately $0.7 million and interest income of approximately

$0.2 million. Other income (expense), net for the year ended December 31, 2013 included $1.0 million in reimbursements from Aerpio for employee-related costs and $2.4 million gain on the extinguishment of debt, partially offset by net interest expense of $0.7 million. The decrease in reimbursements from Aerpio for employee-related costs is principally the result of reduced time spent by our employees on Aerpio related activities. Under the terms of the administrative services agreements entered into upon disposition of Aerpio in 2011, we and Aerpio obtain from, and provide to, each other certain services.

Comparison of the Years Ended December 31, 2013 and 2012

	Year ended December 31,		Increase (Decrease)
	2013	2012	
	(In Thousands)		
Operating expenses:			
Research and development	$10,781	$5,632	$ 5,149
General and administrative	5,152	2,891	2,261
Total operating expenses	15,933	8,523	7,410
Loss from operations	(15,933)	(8,523)	7,410
Other income, net	2,766	327	2,439
Net loss	$(13,167)	$(8,196)	$ 4,971

Research and Development Expenses. Research and development expenses were $10.8 million for the year ended December 31, 2013, compared to $5.6 million for the year ended December 31, 2012, an increase of $5.1 million. The increase was primarily due to an increase in AKB-6548 clinical trial costs of approximately $2.5 million due to the initiation of our Phase 2b study in July 2013 and its continued enrollment, an increase of approximately $1.3 million in drug substance and drug manufacturing costs and increased patent costs of approximately $1.3 million.

General and Administrative Expenses. General and administrative expenses were $5.2 million for the year ended December 31, 2013, compared to $2.9 million for the year ended December 31, 2012. The increase of $2.3 million was primarily due to an increase in stock-based compensation expense of $1.4 million and increased professional fees of $0.5 million indirectly related to the initial public offering. The remaining increase was due to offsetting increases and decreases in all general and administrative costs.

Other Income, Net. Other income, net, was $2.8 million for the year ended December 31, 2013, compared to $0.3 million for the year ended December 31, 2012, an increase of approximately $2.4 million. Other income, net for the year ended December 31, 2013 included $1.0 million in reimbursements from Aerpio for employee-related costs of the Company and a $2.4 million gain on the extinguishment of debt, partially offset by net interest expense of $0.7 million. Other income, net for the year ended December 31, 2012 included $2.0 million in reimbursements from Aerpio for employee-related costs of the Company, partially offset by net interest expense of $1.6 million. The decrease in reimbursements from Aerpio for employee-related costs of the Company is principally the result of reduced time spent by our employees on Aerpio related activities. Under the terms of the administrative services agreements entered into upon disposition of Aerpio by the Company in 2011, the Company and Aerpio obtain from and provide to each other certain services.

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, 2014, we had an accumulated deficit of $100.7 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 from the sale of common stock, preferred stock and convertible notes. As of December 31, 2014, we had cash and cash equivalents and available for sale securities of approximately $108.9 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 and 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,		
	2014	2013	2012
	(In Thousands)		
Net cash provided by (used in):			
Operating activities	$(27,483)	$(11,332)	$(7,211)
Investing activities	(65,352)	(11,425)	1,366
Financing activities	104,400	42,331	2,475
Net increase in cash and cash equivalents	$11,565	$19,574	$(3,370)

Operating Activities. During the years ended December 31, 2014, 2013 and 2012, our operating activities used net cash of $27.5 million, $11.3 million and $7.2 million respectively. The net cash used in operating activities in these periods primarily resulted from our net losses and changes in our working capital accounts. The increase in net cash used in operations for the year ended December 31, 2014 as compared to the year ended December 31, 2013 was due primarily to higher operating expenses during the year ended December 31, 2014 of $37.9 million as compared to $15.9 million for the year ended December 31, 2013 adjusted for non-cash items, including stock-based compensation of $6.0 million in 2014. The increase in net cash used in operations for the year ended December 31, 2013 as compared to the year ended December 31, 2012 was due primarily to higher operating expenses and a $2.4 million gain on the extinguishment of debt during the year ended December 31, 2013.

Investing Activities. During the years ended December 31, 2014 and 2013, our investing activities used net cash of $65.4 million and $11.4 million, respectively and provided cash of $1.4 million during the year ended December 31, 2012. Net cash used in investing activities for the years ended December 31, 2014 and 2013 was comprised primarily of purchases of available for sale securities of and purchases of equipment, offset by proceeds from the maturities of available for sale securities. Net cash provided by investing activities for the year ended December 31, 2012 was $1.4 million and consisted primarily of proceeds from sales of available for sale securities.

Financing Activities. During the years ended December 31, 2014, 2013 and 2012 our net cash provided by financing activities was $104.4 million, $42.3 million and $2.5 million, respectively. Net cash provided by financing activities for the year ended December 31, 2014 consisted primarily of net proceeds from the issuance of common stock in connection with our IPO. Net cash provided by financing activities for the year ended December 31, 2013 and 2012 consisted primarily of net proceeds from the issuance of preferred stock.

Operating Capital Requirements

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

anticipate that we will need substantial additional funding in connection with our continuing operations.

We believe that the net proceeds from our IPO and our existing cash and cash equivalents and available for sale securities will be sufficient to fund our projected operating requirements through the first half of 2016. However, we may require additional capital for the further development of our existing product candidates and may also need to raise additional funds sooner to pursue other 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. Additional capital may not be available on reasonable terms, if at all. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of one or more of our 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 Item 1A Risk Factors of this Annual Report.

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

In December 2013, the Company entered into a three-year lease for 6,837 square feet of office space in Cambridge, Massachusetts. The lease has monthly lease payments of approximately $31,000 for the first twelve months, with annual rent escalation thereafter, and provides a rent abatement of approximately $31,000 for the first full calendar month of the lease term. The lease term commenced in January 2014. The Company has recorded a deferred lease obligation in 2014 which represents the cumulative difference between actual facility lease payments and lease expense recognized ratably over the lease period, which is included in other liabilities. In accordance with the lease, the Company entered into a cash-collateralized irrevocable standby letter of credit in the amount of $125,345, naming the landlord as beneficiary. The Company did not have rent expense associated with this lease in 2013.

In December 2014, the Company entered into a First Amendment to Lease (Amendment) for additional office space contiguous to its current office space in Cambridge, Massachusetts. The Amendment includes leasing an additional 8,530 square feet of office space (Expansion Space), with an estimated occupancy date of March 1, 2015. The Amendment provides for additional monthly lease payments of approximately $45,000 for the 8,530 square feet for the first twelve months and provides for annual rent escalations thereafter. The Amendment includes a Landlord's contribution for leasehold improvements in the amount of approximately $100,000. The Company currently records a deferred lease obligation for the original lease which represents the cumulative difference between actual facility lease payments and lease expense recognized ratably over the lease period also record a deferred lease obligation for the Expansion Space at time of occupancy. The Company has an existing cash-collateralized irrevocable standby letter of credit of $125,345, naming the landlord as beneficiary. In connection with the Amendment, the Company paid an additional cash security deposit to the landlord of $179,130.

We lease office equipment under a three year capital lease with payments commencing in February 2014.

At December 31, 2014, the Company's future minimum payments required under these leases are as follows:

	Payments due by period				
	Total	Less than 1 year	1-3 years	3-5 years	More than 5

					years
Capital Lease Obligations	$8,650	$4,200	$4,450	$ -	$ -
Operating Lease Obligations	1,811,108	875,479	935,629	-	-
Total	$1,819,758	$879,679	$940,079	$ -	$ -

Off-Balance Sheet Arrangements

As of December 31, 2014 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, 2014 and 2013, we had cash and cash equivalents and available for sale securities of $108.9 million and $32.6 million, respectively, primarily money market mutual funds consisting of U.S. government debt securities, certificates of deposit and corporate debt securities. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments are in short-term securities. Our investments are subject to interest rate risk and will fall in value if market interest rates increase. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our portfolio.

Item 8. Financial Statements and Supplementary Data

Akebia Therapeutics, Inc.

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Report of Independent Registered Public Accounting Firm

The Board of Directors and Shareholders of

Akebia Therapeutics, Inc.

We have audited the accompanying consolidated balance sheets of Akebia Therapeutics, Inc. as of December 31, 2014 and 2013, and the related consolidated statements of operations and comprehensive loss, redeemable convertible preferred stock and stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2014. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

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

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Akebia Therapeutics, Inc. at December 31, 2014 and 2013, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2014, in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP

Boston, Massachusetts

March 4, 2015

AKEBIA THERAPEUTICS, INC.

Consolidated Balance Sheets

(in thousands, except share and per share data)

	December 31, 2014	December 31, 2013
Assets		
Current assets:		
Cash and cash equivalents	$32,780	$21,215
Available for sale securities	76,138	11,341
Accounts receivable	48	135
Prepaid expenses and other current assets	1,514	740
Total current assets	110,480	33,431
Property and equipment, net	210	30
Deferred offering costs	—	1,079
Other assets	305	125
Total assets	$110,995	$34,665
Liabilities, redeemable convertible preferred stock and stockholders' equity (deficit)		
Current liabilities:		
Accounts payable	$2,021	$714
Accrued expenses	4,864	3,188
Total current liabilities	6,885	3,902
Other liabilities	32	8
Total liabilities	$6,917	$3,910
Commitments and contingencies (Note 9)		
Redeemable convertible preferred stock; $0.00001 par value; 0 and 5,500,636 shares authorized at December 31, 2014 and December 31, 2013, respectively:		
Series A redeemable convertible preferred stock; 0 and 734,538 shares issued and outstanding at December 31, 2014 and December 31, 2013; (Aggregate liquidation preference of $39,367 at December 31, 2013)	—	39,367
Series B redeemable convertible preferred stock; 0 and 1,287,525 shares issued and outstanding at December 31, 2014 and December 31, 2013; (Aggregate liquidation preference of $21,031 at December 31, 2013)	—	21,257
Series C redeemable convertible preferred stock; 0 and 3,302,885 shares issued and outstanding at December 31, 2014 and December 31, 2013; (Aggregate liquidation preference of $97,203 at December 31, 2013)	—	97,203
Total redeemable convertible preferred stock	$—	$157,827

Stockholders' equity (deficit):		
Preferred stock $0.00001 par value, 25,000,000 and 0 shares authorized at December 31, 2014 and 2013, respectively; 0 shares issued and outstanding at December 31, 2014 and 2013, respectively	—	—
Common stock: $0.00001 par value; 175,000,000 and 14,700,000 shares authorized at December 31, 2014 and 2013, respectively; 20,370,624 and 1,383,345 shares issued and outstanding at December 31, 2014 and 2013, respectively	—	—
Additional paid-in capital	204,969	—
Treasury stock, at cost, 8,463 shares	(162)	—
Accumulated other comprehensive loss	(56)	—
Accumulated deficit	(100,673)	(127,072)
Total stockholders' equity (deficit)	104,078	(127,072)
Total liabilities, redeemable convertible preferred stock and stockholders' equity (deficit)	$110,995	$34,665

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)

	Years ended December 31,		
	2014	2013	2012
Operating expenses:			
Research and development	$25,398	$10,781	$5,632
General and administrative	12,542	5,152	2,891
Total operating expenses	37,940	15,933	8,523
Operating loss	(37,940)	(15,933)	(8,523)
Other income (expense):			
Interest income (expense), net	206	(704)	(1,644)
Extinguishment of debt and other liabilities	—	2,420	—
Reimbursements from Aerpio	700	1,050	1,971
Net loss	$(37,034)	$(13,167)	$(8,196)
Reconciliation of net loss to net loss applicable to common stockholders:			
Net loss	$(37,034)	$(13,167)	$(8,196)
Accretion on preferred stock	(86,899)	(55,886)	(3,323)
Net loss applicable to common stockholders	$(123,933)	$(69,053)	$(11,519)
Net loss per share applicable to common stockholders—basic and diluted	$(8.04)	$(126.94)	$(27.82)
Weighted-average number of common shares used in net loss per share applicable to common stockholders—basic and diluted	15,406,386	544,002	414,107
Comprehensive loss:			
Net loss	$(37,034)	$(13,167)	$(8,196)
Other comprehensive loss:			
Unrealized loss on securities	(56)	—	—
Comprehensive loss	$(37,090)	$(13,167)	$(8,196)

See accompanying notes to consolidated financial statements.

Akebia Therapeutics, Inc.

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

(in thousands, except share and per share data)

mable Convertible Preferred Stock								Stockholders' Equity (Deficit)				
A		Series B		Series C		2012 Series X						
mable rtible		Redeemable Convertible		Redeemable Convertible		Redeemable Convertible						
red Stock er		Preferred Stock		Preferred Stock		Preferred Stock Number		Common Stock	$0.00001	Additional		
s	Amount	Number of Shares	Amount	Number of Shares	Amount	of Shares	Amount	Number of Shares	Par Value	Paid-In Capital	Unrealized Gain/Loss	Accumula Deficit
38	$34,927	1,287,525	$18,659	—	$—	—	$—	563,175	$—	$—	$—	$(48,192
	2,166	—	1,157	—	—	—	—	—	—	(122)	—	(3,200
	—	—	—	—	—	—	—	52,582	—	—	—	—
	—	—	—	—	—	—	—	—	—	122	—	—
	—	—	—	—	—	—	—	—	—	—	—	(8,196
38	37,092	1,287,525	19,816	—	—	—	—	615,757	—	—	—	(59,588
	—	—	—	—	—	—	—	583,126	—	—	—	—
	—	—	—	—	—	—	—	176,717	—	—	—	—

—	—	—	—	—	—	—	14,357	—	5	—	—
—	—	—	—	—	—	—	(6,612)	—	—	—	—
—	—	—	—	—	25,000	2,486	—	—	—	—	—
—	—	—	—	—	25,000	2,458	—	—	—	—	—
—	—	—	2,945,742	40,088	—	—	—	—	—	—	—
—	—	—	357,143	4,944	(50,000)	(4,944)	—	—	—	—	—
2,275	—	1,441	—	52,170	—	—	—	—	(1,569)	—	(54,317
—	—	—	—	—	—	—	—	—	1,564	—	—

	—	—	—	—	—	—	—	—	—	—	—	(13,167
538	39,367	1,287,525	21,257	3,302,885	97,203	—	—	1,383,345	—	—	—	(127,072
	—	—	—	—	—	—	—	6,762,000	—	114,954	—	—
	—	—	—	—	—	—	—	56,000	—	—	—	—
	—	—	—	—	—	—	—	(53,835)	—	—	—	—
	—	—	—	—	—	—	—	—	—	237	—	—
	—	—	—	—	—	—	—	116,394	—	89	—	—
	34,821	—	24,257	—	27,822	—	—	—	—	(85,663)	—	(1,237
538)	(74,188)	(1,287,525)	(45,514)	(3,302,885)	(125,025)	—	—	12,115,183	—	180,057	—	64,670
	—	—	—	—	—	—	—	—	—	6,010	—	—
	—	—	—	—	—	—	—	—	—	(10,715)	—	—
	—	—	—	—	—	—	—	—	—	—	(56)	—
	—	—	—	—	—	—	—	(2,553)	—	—	—	—
	—	—	—	—	—	—	—	(5,910)	—	—	—	—

—	—	—	—	—	—	—	—	—	—	—	(37,034
$—	—	$—	—	$—	—	$—	20,370,624	$—	$204,969	$(56)	$(100,67

See accompanying notes to consolidated financial statements

AKEBIA THERAPEUTICS, INC.

Consolidated Statements of Cash Flows

(in thousands)

	Year ended December 31,		
	2014	2013	2012
Operating activities:			
Net loss	$(37,034)	$(13,167)	$(8,196)
Adjustments to reconcile net loss to net cash used in operating activities:			
Gain on extinguishment of debt and other liabilities	—	(2,420)	—
Depreciation expense	49	1	—
Amortization of debt issuance costs	—	8	17
Amortization of premium/discount on investments	268	752	1,654
Stock-based compensation expense	6,010	1,564	122
Changes in operating assets and liabilities:			
Accounts receivable	87	(50)	(4)
Prepaid expenses and other current assets	(773)	(167)	244
Other assets	(179)	(125)	—
Accounts payable and accrued expenses	4,061	2,272	(1,048)
Other liabilities	28	—	—
Net cash used in operating activities	(27,483)	(11,332)	(7,211)
Investing activities:			
Purchase of equipment	(229)	(19)	—
Proceeds from maturities of available for sale securities	12,585	1,990	—
Proceeds from sale of available for sale securities	—	—	1,366
Purchases of available for sale securities	(77,708)	(13,395)	—
Net cash used in investing activities	(65,352)	(11,425)	1,366
Financing activities:			
Proceeds from issuance of redeemable convertible preferred stock, net of issuance costs	—	40,047	—
Proceeds from issuance of 2012 Series X preferred stock, net of issuance costs	—	2,279	2,475
Repurchase of treasury stock	(162)	—	—
Proceeds from issuance of common stock, net of issuance costs	104,328	5	—
Proceeds from receipt of payment on promissory notes issued in exchange for shares of common stock	237	—	—
Payments on capital lease obligations	(3)	—	—
Net cash provided by financing activities	104,400	42,331	2,475
Increase in cash and cash equivalents	11,565	19,574	(3,370)
Cash and cash equivalents at beginning of period	21,215	1,641	5,011
Cash and cash equivalents at end of period	$32,780	$21,215	$1,641
Non-cash financing activities:			

Conversion of series A, series B and series C preferred stock into common stock	$244,727	$—	$—
Accretion of preferred stock to redemption value	$86,899	$55,886	$3,323
Unpaid initial public offering issuance costs	$—	$857	$—
Assets acquired under capital lease	$—	$12	$—
Reclassification of 2012 Series X preferred stock from debt to preferred stock	$—	$2,486	$—
Conversion of 2012 Series X preferred stock into Series C preferred stock	$—	$4,944	$—

See accompanying notes to consolidated financial statements.

Akebia Therapeutics, Inc.

Notes to Consolidated Financial Statements

1. Nature of Organization and Operations

Akebia Therapeutics, Inc. (Akebia, or the Company) is a biopharmaceutical company focused on delivering innovative therapies to patients with kidney disease through the biology of hypoxia-inducible factor (HIF). HIF is the primary regulator of the production of red blood cells in the body and a potentially novel mechanism of treating anemia. The Company's lead product candidate, AKB-6548, is being developed as a once-daily, oral therapy that has successfully completed a Phase 2b study demonstrating that AKB-6548 can safely and predictably raise hemoglobin levels in non-dialysis patients with anemia related to chronic kidney disease (CKD).

The Company's operations to date have been limited to organizing and staffing the Company, business planning, raising capital, acquiring and developing its technology, identifying potential product candidates and undertaking preclinical and clinical studies. The Company has not generated any product revenue to date, nor is there any assurance of any future product revenue. The Company's product candidates are subject to long development cycles and there is no assurance the Company will be able to successfully develop, obtain regulatory approval for or market its product candidates.

The Company is subject to a number of risks including, but not limited to, the need to obtain adequate additional funding, possible failure of preclinical testing or clinical trials, the need to obtain marketing approval for its product candidates, the development of new technological innovations by competitors, the need to successfully commercialize and gain market acceptance of any of the Company's products that are approved and the ability to protect its proprietary technology. If the Company does not successfully commercialize any of its products, it will be unable to generate product revenue or achieve profitability.

The Company believes that it can continue as a going concern as its cash resources of approximately $108.9 million at December 31, 2014 will be sufficient to allow the Company to fund its current operating plan through the required minimum period of at least the next twelve months. There can be no assurance, however, that the current operating plan will be achieved in the timeframe 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.

Unless otherwise indicated, all information in these financial statements gives retrospective effect to the 1.75-for-1 stock split of the Company's common stock (the Stock Split) that was effected on March 6, 2014 (see Note 7), as well as any other stock-splits in historical periods.

The Company was incorporated on February 27, 2007 under the laws of the State of Delaware.

2. Summary of Significant Accounting Policies

Initial Public Offering

On March 25, 2014, the Company completed its initial public offering (IPO) whereby the Company sold 6,762,000 shares of common stock including 879,647 shares of common stock pursuant to the full exercise of an over-allotment option granted to the underwriters in connection with the offering at a price of $17.00 per share. The shares began

trading on the Nasdaq Global Market on March 20, 2014. The aggregate net proceeds received by the Company from the offering were $104,364,560, net of underwriting discounts and commissions and estimated offering expenses payable by the Company. Upon the closing of the IPO, all outstanding shares of convertible redeemable preferred stock converted into 12,115,183 shares of common stock. As of March 25, 2015, the Company is authorized to issue 175,000,000 shares of common stock and 25,000,000 shares of undesignated preferred stock.

Our preferred stock was redeemable at the greater of fair value or the original issuance price. We recorded $86,899,555 of accretion on the preferred stock in the period from January 1, 2014 through the date of the closing of our IPO which represents the difference in the carrying value at December 31, 2013 and the fair value of the preferred stock just prior to conversion into common stock.

Basis of Presentation

The accompanying consolidated financial statements include the accounts of the Company and its wholly-owned subsidiary, Akebia Therapeutics Securities Corporation. 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 (“GAAP”). Any reference in these notes to applicable guidance is meant to refer to the authoritative United States generally accepted accounting principles as found in the Accounting Standards Codification (“ASC”) and Accounting Standards Update (“ASU”) of the Financial Accounting Standards Board (“FASB”).

Recent Accounting Pronouncements

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

In June 2014, the FASB issued ASU No. 2014-10, which eliminates the concept of a development stage entity, or DSE, in its entirety from GAAP. Under existing guidance, DSEs are required to report incremental information, including inception-to-date financial information, in their financial statements. A DSE is an entity devoting substantially all of its efforts to establishing a new business and for which either planned principal operations have not yet commenced or have commenced but there has been no significant revenues generated from that business. Entities classified as DSEs will no longer be subject to these incremental reporting requirements after adopting ASU No. 02014-10. ASU No. 2014-10 is effective for fiscal years beginning after December 15, 2014, with early adoption permitted. Retrospective application is required for the elimination of incremental DSE disclosure. Prior to the issuance of ASU No. 2014-10, the Company had met the definition of a DSE since its inception. The Company elected to adopt this ASU early and, therefore, it has eliminated the incremental disclosures previously required of DSEs, starting with the Quarterly Report on Form 10-Q for the quarter ended June 30, 2014 (File No. 001-36352), which was filed with the SEC on August 11, 2014.

Segment Information

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

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results may differ from those estimates. Management considers many factors in selecting appropriate financial accounting policies and controls, and in developing the estimates and assumptions that are used in the preparation of these financial statements. Management must apply significant judgment in this process. In addition, other factors may affect estimates, including: expected business and operational changes, sensitivity and volatility associated with the assumptions used in developing estimates, and whether historical trends are expected to be representative of future trends. The estimation process often may yield a range of potentially reasonable estimates of the ultimate future outcomes, and management must select an amount that falls within that range of reasonable estimates. Estimates are used in the following areas, among others: stock-based compensation expense, fair value of common stock and preferred stock and the Company’s other equity instruments (in periods prior to the IPO), accrued expenses, prepaid expenses and income taxes.

Prior to the IPO, the Company utilized significant estimates and assumptions in determining the fair value of its common stock. The Company granted stock options at exercise prices not less than the fair market value of its common stock as determined by the Board of Directors contemporaneously at the date such grants were made, with input from management. For periods prior to March 2014, the fair value of common stock at the grant date was

adjusted in connection with the Company's retrospective fair value assessment for financial reporting purposes. Prior to the Company's IPO, the Board of Directors determined the estimated fair value of the Company's common stock based on a number of objective and subjective factors, including external market conditions affecting the biotechnology industry sector and the prices at which the Company sold shares of preferred stock, the superior rights and preferences of securities senior to the Company's common stock at the time and the likelihood of achieving a liquidity event, such as an IPO or sale of the Company.

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

Cash and Cash Equivalents

Cash and cash equivalents consist of all cash on hand, deposits and funds invested in available for sale securities with original maturities of three months or less at the time of purchase. At December 31, 2014, the Company's cash is primarily in money market funds. The Company may maintain balances with its banks in excess of federally insured limits.

Investments

Management determines the appropriate classification of securities at the time of purchase and reevaluates such designation as of each balance sheet date. Currently, the Company classifies all securities as available-for-sale which are included in current assets as they are intended to fund current operations. The Company carries available-for-sale securities at fair value, with temporary unrealized gains and losses, reported in accumulated other comprehensive income, a component of stockholders' equity (deficit). 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. Unrealized losses on available-for-sale securities that are determined to be temporary, and not related to credit loss, are recorded, net of tax, in accumulated other comprehensive income. 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 (expense), net" within the Consolidated Statements of Operations and Comprehensive Loss. We also include 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.

Research and Development

Costs incurred in connection with research and development activities are expensed as incurred. Research and development expenses consist of (i) employee-related expenses, including salaries, benefits, travel and stock-based compensation expense; (ii) external research and development expenses incurred under arrangements with third parties, such as contract research organizations, investigational sites and consultants; (iii) the cost of acquiring, developing and manufacturing clinical study materials; (iv) facilities and other expenses, which include direct and allocated expenses for rent and maintenance of facilities; and (v) costs associated with preclinical and clinical activities and regulatory operations.

The Company enters into consulting, research and other agreements with commercial firms, researchers, universities and others for the provision of goods and services. Under such agreements, the Company may pay for services on an hourly, monthly, quarterly, project or other basis. Such arrangements are generally cancellable upon reasonable notice and payment of costs incurred. Costs are considered incurred based on an evaluation of the progress to completion of specific tasks under each contract using information and data provided to us by the Company's clinical sites and vendors. These costs consist of direct and indirect costs associated with specific projects, as well as fees paid to various entities that perform certain research on behalf of the Company.

Patents

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

Income Taxes

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

The Company 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, 2014 and 2013, the Company does not have any

significant uncertain tax positions. The Company recognizes interest and penalties related to uncertain tax positions in income tax expense.

Stock-Based Compensation

The Company accounts for its stock-based compensation awards in accordance with FASB ASC Topic 718, Compensation—Stock Compensation (ASC 718). ASC 718 requires all stock-based payments to employees, including grants of employee stock options 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. The Company accounts for stock-based awards to non-employees in accordance with FASB ASC Topic 505-50, Equity-Based Payments to Non-Employees (ASC 505-50), which requires the fair value of the award to be re-measured at fair value until a performance commitment is reached or counterparty performance is complete. The Company's stock-based awards are comprised of stock options, shares of restricted stock and shares of common stock. The Company estimates the fair value of options granted using the Black-Scholes option pricing model. The Company uses the value of its common stock 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 a public market for the trading of the Company's common stock and a lack of company-specific historical and implied volatility data, the Company has based its estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. The historical volatility is calculated based on a period of time commensurate with the expected term assumption. The computation of expected volatility is based on the historical volatility of a representative group of companies with similar characteristics to the Company, including stage of product development and life science industry focus. The Company is in a very early stage of product development with no revenue and the representative group of companies has certain similar characteristics to the Company. The Company believes the group selected has sufficient similar economic and industry characteristics, and includes companies that are most representative of the Company The Company uses the simplified method as prescribed by the SEC Staff Accounting Bulletin No. 107, Share-Based Payment, to calculate the expected term for options granted to employees as it does not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. The expected term is applied to the stock option grant group as a whole, as the Company does not expect substantially different exercise or post-vesting termination behavior among its employee population. For options granted to non-employees, the Company utilizes the contractual term of the arrangement as the basis for the expected term assumption. The risk-free interest rate is based on a treasury instrument whose term is consistent with the expected life of the stock options. The expected dividend yield is assumed to be zero as the Company has never paid dividends and has no current plans to pay any dividends on its common stock, which is similar to the Company's peer group.

The Company's stock-based awards are subject to either service- or performance-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. Compensation expense related to awards to employees with performance-based vesting conditions is recognized based on the grant date fair value over the requisite service period using the accelerated attribution method to the extent achievement of the performance condition is probable. Consistent with the guidance in ASC 505-50, compensation expense related to awards to non-employees with performance-based vesting conditions is recognized based on the then-current fair value at each financial reporting date prior to the measurement date over the requisite service period using the accelerated attribution method to the

extent achievement of the performance condition is probable.

The Company is also required to estimate forfeitures at the time of grant, and revise those estimates in the subsequent periods if actual forfeitures differ from its estimates. The Company uses historical data to estimate pre-vesting forfeitures and record stock-based compensation expense only for those awards that are expected to vest. To the extent that actual forfeitures differ from the Company's estimates, the difference is recorded as a cumulative adjustment in the period the estimates were revised. Stock-based compensation expense recognized in the financial statements is based on awards that are ultimately expected to vest.

Fair Value of Financial Instruments

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

Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's assumptions about the inputs that market participants would use in pricing the asset or liability, and are developed based on the best information available in the circumstances. The fair value hierarchy applies only to the valuation inputs used in determining the reported fair value of the investments, and is not a measure of the investment credit quality. The three levels of the fair value hierarchy are described below:

Level 1 – Valuations based on unadjusted quoted prices in active markets for identical assets or liabilities that the Company has the ability to access at the measurement date.
Level 2 – Valuations based on quoted prices for similar assets or liabilities in markets that are not active, or for which all significant inputs are observable, either directly or indirectly.
Level 3 – Valuations that require inputs that reflect the Company's own assumptions that are both significant to the fair value measurement and unobservable.
To the extent that valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

Items measured at fair value on a recurring basis include short-term investments (see Note 5). The carrying amounts of accounts receivable, 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, investments and accounts receivable are the only financial instruments that potentially subject the Company to concentrations of credit risk. The Company maintains its cash with high quality, accredited financial institutions and, accordingly, such funds are subject to minimal credit risk. The Company has no significant off-balance sheet concentrations of credit risk, such as foreign currency exchange contracts, option contracts or other hedging arrangements.

Net Loss per Share

Basic net loss per share is calculated by dividing net loss attributable to common stockholders by the weighted-average shares outstanding during the period, without consideration for common stock equivalents. Diluted net loss per share is calculated by adjusting weighted-average shares outstanding for the dilutive effect of common stock equivalents outstanding for the period, determined using the treasury-stock method. For purposes of the diluted net loss per share calculation, preferred stock, stock options and unvested restricted stock are considered to be common stock equivalents, but have been excluded from the calculation of diluted net loss per share, as their effect would be anti-dilutive for all periods presented. Therefore, basic and diluted net loss per share were the same for all periods presented.

Property and Equipment

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

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

The following is the summary of property and equipment and related accumulated depreciation as of December 31, 2014 and December 31, 2013.

	Useful Life	December 31, 2014	2013
Computer equipment and software	3	$98,700	$19,732
Furniture and fixtures	5	117,157	—
Equipment	7	6,195	—
Leasehold improvements	Shorter of the useful life or remaining lease term (3 years)	26,605	—
Office equipment under capital lease	3	11,916	11,916
		260,573	31,648
Less accumulated depreciation		(50,645)	(1,282)
Net property and equipment		$209,928	$30,366

Depreciation expense, including expense associated with assets under capital leases, was $49,363, $1,282 and $0 for the years ended December 31, 2014, 2013 and 2012, respectively.

3. Distribution of Aerpio Therapeutics, Inc.

On December 22, 2011, the Company assigned certain assets and liabilities to a wholly-owned subsidiary, Aerpio Therapeutics, Inc. (Aerpio), which has since operated as an independent, stand-alone company and is no longer a wholly-owned subsidiary. The assigned assets and liabilities included all of the Company’s fixed assets, the Company’s Tie2 activator program, AKB-9778, for diabetic macular edema, the HIF-1 stabilizer program, AKB-4924, for inflammatory bowel disease and contracts, intellectual property, current assets and current liabilities associated with these programs. The Aerpio shares were then distributed to the Company’s shareholders as a distribution on the basis of one share of Aerpio Series A Preferred Stock for every 35 shares of Akebia Series A Preferred Stock owned, one share of Aerpio Series A Preferred Stock for every 100 shares of Akebia Series B Preferred Stock owned, and one share of Aerpio Common Stock for every 175 shares of Akebia Common Stock owned.

Under the terms of administrative services agreements, the Company and Aerpio obtain from and provide to each other certain services beginning in 2012, and as outlined below. These agreements are cancellable upon mutual agreement or a sale of either company.

Below is a summary of the activities included in the statements of operations and comprehensive loss:

Activity	Financial Statement Caption	Year ended December 31, 2014	2013
Reimbursement from Aerpio for Akebia employee costs	Reimbursements from Aerpio	$ 700,233	$ 1,049,844
Facility-related charges from Aerpio	General and administrative Operating expenses	$ 68,813	$ 277,923

Below is a summary of the receivables and payables included in the balance sheets related to Aerpio:

Activity	Financial Statement Caption	Year Ended December 31, 2014	2013
Amounts receivable from Aerpio	Accounts receivables	$48,135	$135,339
Amounts payable to Aerpio	Accounts payable	$3,561	$62,735

4. Available for sale securities

Available for sale securities at December 31, 2014 and December 31, 2013 consist of the following:

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
December 31, 2014				
Cash and cash equivalents:				
Cash and money market account	$ 32,780,113	$ —	$ —	$ 32,780,113
Total cash and cash equivalents	$ 32,780,113	$ —	$ —	$ 32,780,113
Available for sale securities:				
Certificates of deposit	13,429,004	—	—	$ 13,429,004
U.S. Government debt securities	38,412,150	1,427	(28,290)	38,385,287
Commercial paper	2,499,264	—	—	2,499,264
Corporate debt securities	21,853,974	2,437	(31,932)	21,824,479
Total available for sale securities	$ 76,194,392	$ 3,864	$ (60,222)	$ 76,138,034
Total cash, cash equivalents, and available for sale securities	$ 108,974,505	$ 3,864	$ (60,222)	$ 108,918,147

The estimated fair value of the Company’s available for sale securities balance at December 31, 2014, by contractual maturity, is as follows:

Due in one year or less	$ 36,283,628
Due after one year	39,854,406
Total available for sale securities	$ 76,138,034

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
December 31, 2013				
Cash and cash equivalents:				
Cash and money market account	$ 21,215,228	$ —	$ —	$ 21,215,228
Total cash and cash equivalents	$ 21,215,228	$ —	$ —	$ 21,215,228
Available for sale securities:				
Certificates of deposit	$ 1,330,132	$ —	$ —	$ 1,330,132
U.S. Government debt securities	7,506,951	2,418	—	7,509,369
Corporate debt securities	2,501,686	54	—	2,501,740

Total available for sale securities	$ 11,338,769	$ 2,472	$ —	$ 11,341,241
Total cash, cash equivalents, and available for sale securities	$ 32,553,997	$ 2,472	$ —	$ 32,556,469

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 marketable securities within Level 1 or Level 2. This is because the Company values its cash equivalents and marketable 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, 2014 are summarized below:

	Fair Value Measurements Using			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash and cash equivalents	32,780,113	$—	$ —	$32,780,113
Certificates of deposit	—	13,429,004	—	$13,429,004
U.S. Government debt securities	—	38,385,287	—	$38,385,287
Commercial paper	—	2,499,264	—	$2,499,264
Corporate debt securities	—	21,824,479	—	$21,824,479
	$32,780,113	$76,138,034	$ —	$108,918,147

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

Assets measured or disclosed at fair value on a recurring basis as of December 31, 2013 are summarized below:

	Fair Value Measurements Using			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash and cash equivalents	$21,215,228	$—	$ —	$21,215,228
Certificates of deposit	—	1,330,132	—	1,330,132
U.S. Government debt securities	—	7,509,369	—	7,509,369
Corporate debt securities	—	2,501,740	—	2,501,740
	$21,215,228	$11,341,241	$ —	$32,556,469

The Company had no assets or liabilities measured at fair value on a recurring basis using significant unobservable inputs (Level 3) at December 31, 2014 and December 31, 2013.

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, 2014	December 31, 2013
Professional fees	2,459,308	$ 2,452,067
Accrued bonus	1,286,127	439,435
Accrued vacation	177,162	109,921
Accrued severance	178,819	—
Accrued payroll	213,224	—
Other	549,145	186,338
Total accrued expenses	$4,863,785	$ 3,187,761

In February 2014, the Company entered into a separation agreement with an employee primarily as a result of the transition to the Company's Cambridge, Massachusetts location. During the first quarter of 2014, the Company recorded severance expense in the amount of $323,685, which was recorded to general and administrative expense. During the year ended December 31, 2014, approximately $271,000 was paid out of the severance accrual. At December 31, 2014, $45,890 remained in accrued expenses in relation to the unpaid severance costs, which will be paid out through February 2015.

In August 2014, the Company entered into a separation agreement with an employee, which became effective on August 13, 2014. The Company will record the expense and liability associated with the separation agreement ratably over the period from August 5, 2014 through December 31, 2015 because the severance payments are subject to continued service and forfeiture until December 31, 2015. During the year ended 2014, the Company recorded severance expense in the amount of $118,852, which was recorded to research and development expense and will be paid out beginning January 2015 through December 2015.

7. Stockholders' Equity

As of December 31, 2014, the authorized capital stock of the Company included 175,000,000 shares of common stock, par value $0.00001 per share and 25,000,000 shares of undesignated preferred stock, par value $0.00001 per share.

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.

As of December 31, 2013, the authorized capital stock of the Company included 5,500,636 shares of preferred stock, par value $0.00001 per share, of which: (i) 734,538 shares were designated as Series A redeemable convertible preferred stock (Series A Redeemable Convertible Preferred Stock), (ii) 1,287,525 shares were designated as Series B redeemable convertible preferred stock (Series B Redeemable Convertible Preferred Stock), (iii) 3,428,572 shares were designated as Series C redeemable convertible preferred stock (Series C Redeemable Convertible Preferred Stock) and (iv) 50,001 shares were designated as Series X convertible preferred stock (Series X Convertible Preferred Stock). There is no outstanding Series X Convertible Preferred Stock as of December 31, 2013. The Series A Redeemable Convertible Preferred Stock, the Series B Redeemable Convertible Preferred Stock and the Series C Redeemable Convertible Preferred Stock are collectively referred to as the Redeemable Convertible Preferred Stock.

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.

Reserved for Future Issuance

As of December 31, 2014 and December 31, 2013 based on the authorized shares for each series, the Company has reserved the following shares of common stock for future issuance:

	December 31, 2014	December 31, 2013
Conversion of Series A Redeemable Convertible Preferred Stock	—	3,672,673
Conversion of Series B Redeemable Convertible Preferred Stock	—	2,253,157
Conversion of Series C Redeemable Convertible Preferred Stock	—	6,296,451
Options to purchase common stock	1,526,346	1,251,398
Shares available for future issuance	1,549,154	155,108
Total	3,075,500	13,628,787

8. Income Taxes

These was no current or deferred income tax expense or benefit for the years ended December 31, 2014 and 2013, 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 tax with the provision for income taxes, follow:

	Year ended December 31,	
	2014	2013
Federal tax at statutory rate	34.0 %	34.0 %
State and local tax at statutory rate	5.5	0.8
Research and development tax credits	(0.6)	4.2
Disqualified interest expense	0.0	(1.9)
Cancellation of debt income	0.0	6.2
Equity Compensation	(1.6)	(2.6)
Other permanent differences and credits	(0.1)	0.0
Change in valuation allowance	(37.2)	(40.7)
Effective tax rate	0.0 %	0.0 %

The Company's income tax provision was computed based on the federal statutory rate and the average state statutory rates, net of the related federal benefit.

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. Significant components of the Company's deferred tax assets and liabilities are as follows:

	December 31, 2014	December 31, 2013
Deferred tax assets:		
Current		
Accrued expenses	$558,935	$189,648
Less valuation allowance	(558,935)	
Net current deferred tax asset	-	189,648
Noncurrent		
Intangible assets	603,644	602,784
Restricted stock	436,058	-
Fixed assets	1,690	-
Research and development credits	1,588,897	1,821,403
Net operating loss carryforward	30,558,915	17,916,817
Other	479,283	24,371
Less valuation allowance	(33,668,487)	(20,446,542)
Net noncurrent deferred tax assets	-	(81,167)
Total deferred tax assets, net of valuation allowance	-	108,481
Deferred tax liabilities:		
Fixed assets	-	(925)
Restricted stock	-	(107,556)
Total deferred tax liabilities	-	(108,481)
Net deferred tax asset	$-	$-

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.

At December 31, 2014 and December 31, 2013, the Company has approximately $1,181,000 (after amortization of $788,000) and $1,312,000 (after amortization of $656,000), respectively, of start-up expenses capitalized for income tax purposes with amortization available to offset future federal, state and local income tax. Additionally, at December 31, 2014 and 2013, the Company has approximately $84,200,000 and $51,630,000, respectively, of net operating loss (NOL) carry-forwards. Included in the 2014 NOL are tax deductions related to equity compensation in excess of book compensation expense. Pursuant to the realization requirements in ASC 718, these tax deductions are not included in the NOL deferred tax asset above. The Company also has approximately $1,654,000 of federal and state research and development tax credit carry-forwards. The NOL and research and development tax credit carry-forwards begin to expire in 2027, and will be utilized for tax purposes at such time the Company generates taxable income.

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 carry-forwards may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant shareholders over a three-year period in excess of 50%, as defined under Sections 382 and 383 of the Internal Revenue Code, respectively, as well as similar state provisions. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the value of the Company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. The Company has completed

several financings since its inception, which may have resulted in a change in control as defined by Sections 382 and 383 of the Internal Revenue Code, or could result in a change in control in the future.

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, 2014 and 2013, 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. The Company's 2011 through 2013 tax years remain open and subject to examination by federal and state taxing authorities. However, federal and state net operating losses from 2007 through 2013 are subject to review by taxing authorities in the year utilized.

9. Commitments and Contingencies

In December 2013, the Company entered into a three-year lease for 6,837 square feet of office space in Cambridge, Massachusetts. The lease has monthly lease payments of approximately $31,000 for the first twelve months, with annual rent escalation thereafter, and provides a rent abatement of approximately $31,000 for the first full calendar month of the lease term. The lease term commenced and rental payments began in January 2014. The Company has recorded a deferred lease obligation in 2014 which represents the cumulative difference between actual facility lease payments and lease expense recognized ratably over the lease period, which is included in other liabilities. In accordance with the lease, the Company entered into a cash-collateralized irrevocable standby letter of credit in the amount of $125,345, naming the landlord as beneficiary. The Company did not have rent expense associated with this lease in 2013.

In December 2014, the Company entered into a First Amendment to Lease (Amendment) for additional office space contiguous to its current office space in Cambridge, Massachusetts. The Amendment includes leasing an additional 8,530 square feet of office space (Expansion Space), with an estimated occupancy date of March 1, 2015. The Amendment provides for additional monthly lease payments of approximately $45,000 for the 8,530 square feet for

the first twelve months and provides for annual rent escalations thereafter. The monthly rent on the existing 6,837 square feet will remain at approximately $32,000 through December 31, 2016, the expiration of the lease. The Amendment includes a Landlord's contribution for leasehold improvements in the amount of approximately $100,000 which will be accounted for as a reduction in monthly rent expense over the term of the lease. The Company currently records a deferred lease obligation for the original lease which represents the cumulative difference between actual facility lease payments and lease expense recognized ratably over the lease period and will also record a deferred lease obligation for the Expansion Space at time of occupancy. The Company has an existing cash-collateralized irrevocable standby letter of credit of $125,345, naming the landlord as beneficiary. In connection with the Amendment, the Company paid an additional cash security deposit to the landlord of $179,130. These amounts are included in other assets.

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

At December 31, 2014, the Company's future minimum payments required under these leases are as follows:

	Operating Lease	Capital Lease	Total
2015	$875,479	$4,200	$879,679
2016	$935,629	4,200	$939,829
2017	—	250	250
Total	$1,811,108	8,650	$1,819,758
Less amount representing interest		(297)	
Present value of minimum lease payments at December 31, 2014		$8,353	

The Company recorded $377,578 and $0 in rent expense for the years ended December 31, 2014 and 2013 respectively.

The Company contracts with various organizations to conduct research and development activities with remaining contract costs to the Company of approximately $4,312,081 and $4,477,081 at December 31, 2014 and December 31, 2013, respectively. The scope of the services under the 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.

10. Stock-Based Compensation

On February 28, 2014, the Company's Board of Directors adopted its 2014 Incentive Plan (2014 Plan), which was subsequently approved by its stockholders and became effective upon the closing of the Company's IPO on March 25, 2014. The 2014 Plan replaces the 2008 Equity Incentive Plan (2008 Plan).

The 2014 Plan allows for the granting of stock options, stock appreciation rights, or SARs, restricted stock, unrestricted stock, stock units, performance awards and other awards convertible into or otherwise based on shares of our common stock. Dividend equivalents may also be provided in connection with an award under the 2014 Plan. The Company's employees, officers, directors and consultants and advisors are eligible to receive awards under the 2014 Plan. The Company initially reserved 1,785,000 shares of its common stock for the issuance of awards under the 2014 Plan. The 2014 Plan provides that the number of shares reserved and available for issuance under the 2014 Plan will automatically increase annually on January 1st of each calendar year, by an amount equal to three percent (3%) of the number of shares of stock outstanding on a fully diluted basis as of the close of business on the immediately preceding December 31st. The 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). Subject to adjustment, no more than 1,131,937 shares of our common stock may be delivered in satisfaction of incentive stock options awarded under the 2014 Plan.

Any options or awards outstanding under the 2008 Plan at the time of adoption of the 2014 Plan remain outstanding and effective. As of December 31, 2014, the total number of common shares that may be issued under all equity award plans is 3,075,500 and approximately 1,549,154 shares remain available for future grants.

During the year ended December 31, 2014, the Company granted 437,289 stock options to employees, 77,525 stock options to directors and 56,000 shares of restricted stock to a former employee.

Stock Options

Options granted by the Company vest over periods of between 12 and 48 months. Options vest in installments of (i) 25% at the one year anniversary and (ii) in either 36 or 48 equal monthly or 12 equal quarterly installments beginning in the thirteenth month after the initial Vesting Commencement Date (as defined) or grant date, subject to

the employee's continuous service with the Company.. Options generally expire ten years after the date of grant.

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,	
	2014	2013
Risk-free interest rate	1.63% - 2.06%	1.71% - 2.03%
Dividend yield	0.00%	0.00%
Volatility	67.97% - 77.00%	75.00% - 79.00%
Expected term (years)	6.25	6.25

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

	Shares	Weighted-Average Exercise Price	Weighted-Average Contractual Life (in years)	Aggregate Intrinsic Value
Outstanding, December 31, 2013	1,251,401	$ 1.01		$8,020,065
Granted	514,814	$ 22.53		
Exercised	(116,394)	$ 0.76		$1,991,922
Forfeited	(123,472)	$ 9.93		$330,223
Expired/cancelled	—			
Outstanding, December 31, 2014	1,526,349	$ 7.57	8.45	$11,523,531
Options exercisable, December 31, 2014	455,130	$ 0.81	7.01	$4,931,055
Expected to vest, December 31, 2014	1,281,733	$ 8.85	9.03	$8,886,570

As of December 31, 2014, there was approximately $8,653,037 of unrecognized compensation cost related to stock options, which is expected to be recognized over a weighted average period of 3.19 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 awards of restricted stock contain a performance condition wherein the vesting commencement date is contingent upon the Company's consummation of a liquidity event, as defined, prior to the fifth anniversary of the date of grant. Certain of the awards of restricted stock have a requisite service period that was complete upon grant. The remainder of the awards of restricted stock have a requisite service period of four years whereby the award vests 25% on the one year anniversary of the 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, recognition of compensation cost did not begin until the occurrence of a liquidity event, as defined. The liquidity event occurred upon the closing of the IPO on March 25, 2014.

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

	Shares	Weighted-Average Grant Date Fair Value
Unvested balance, December 31, 2013	629,512	$ 8.55
Granted	56,000	$ 12.09
Vested	(209,532)	$ 9.16
Forfeited	(53,835)	$ 7.42
Outstanding, December 31, 2014	422,145	$ 9.12

As of December 31, 2014, there was approximately $1,892,185 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 IPO on March 25, 2014. The expense is expected to be recognized over a weighted average period of 1.74 years.

Common Stock

In connection with the termination of a former employee in September 2013, the Company granted the former employee stock awards totaling 70,964 shares in September 2013 and 105,753 shares in December 2013 of Common Stock, at a fair value of $3.77 per share and $7.42 per share, respectively. The fair value of the awards are based on the estimated fair value of the Company's Common Stock at the date of grant. Accordingly, compensation cost was recognized in full on the date of grant. The associated common shares immediately vested, and were not subject to any other restriction. Accordingly, the compensation cost was recognized in full on the date of grant. Total compensation cost of approximately $1,053,000 was recognized during the year ended December 31, 2013 related to these awards.

Compensation Expense Summary

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

	Year ended December 31,	
	2014	2013
Research and development	$2,766,046	$110,686
General and administrative	3,244,005	1,453,073
Total	$6,010,051	$1,563,759

Compensation expense by type of award:

	Year ended December 31,	
	2014	2013
Stock options	$1,924,921	$305,452
Restricted stock	4,085,130	1,258,307
Total	$6,010,051	$1,563,759

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

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 no contributions were made during the year ended December 31, 2014 or 2013.

12. Net Loss per Share

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

	Year ended December 31,	
	2014	2013
Numerator:		
Net loss	$(37,034,039)	$(13,167,180)
Accretion on preferred stock	(86,899,555)	(55,885,844)
Net loss applicable to common stockholders	$(123,933,594)	$(69,053,024)
Denominator:		
Weighted-average number of common shares – basic and diluted	15,406,386	544,002
Net loss per share applicable to common stockholders – basic and diluted	$(8.04)	$(126.94)

The amounts 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,	
	2014	2013
Preferred stock	—	12,002,329
Outstanding stock options	1,526,346	1,251,398
Unvested restricted stock	422,145	629,512
Total	1,948,491	13,883,239

13. Accumulated Other Comprehensive Loss

The following table summarizes the changes in the accumulated balances for each component of accumulated other comprehensive loss, net of tax:

	Unrealized Loss on Investments	Total
Balance at December 31, 2013	$ —	$—

Other comprehensive loss before reclassifications	(56,358)	(56,358)
Net current-period other comprehensive loss	(56,358)	(56,358)
Balance at December 31, 2014	$ (56,358)	$ (56,358)

14. Quarterly Results (unaudited)

	Three Months Ended			
	March 31, 2013	June 30, 2013	September 30, 2013	December 31, 2013
	(in thousands, except per share data) (unaudited)			
Operating expenses	$2,577	$3,121	$ 4,034	$6,201
Loss from operations	$(2,577)	$(3,121)	$ (4,034)	$(6,201)
Other income (expense), net	$1,956	$290	$ 266	$254
Net loss	$(621)	$(2,831)	$ (3,768)	$(5,947)
Net loss per share applicable to common stockholders, basic and diluted	$(3.09)	$(103.19)	$ (11.92)	$(13.92)

	Three Months Ended			
	March 31, 2014	June 30, 2014	September 30, 2014	December 31, 2014
	(in thousands, except per share data) (unaudited)			
Operating expenses	$9,909	$7,840	$ 9,584	$10,607
Loss from operations	$(9,909)	$(7,840)	$ (9,584)	$(10,607)
Other income (expense), net	$212	$222	$ 236	$237
Net loss	$(9,697)	$(7,618)	$ (9,348)	$(10,370)
Net loss per share applicable to common stockholders, basic and diluted	$(43.37)	$(0.39)	$ (0.47)	$(0.52)

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

None.

Item 9A. Controls and Procedures
Controls and Procedures

Management's Annual Report on Internal Control over Financial Reporting

This annual report does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of the company's independent registered public accounting firm due to the existence of a transition period, established by rules of the Securities and Exchange Commission, for newly public companies.

Management's Evaluation of our Disclosure Controls and Procedures

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

As of December 31, 2014, our management, with the participation of our principal executive officer and principal financial officer, evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934). Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives, and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Our principal executive officer and principal financial officer have concluded based upon the evaluation described above that, as of December 31, 2014, our disclosure controls and procedures were effective at the reasonable assurance level.

Changes in Internal Control over Financial Reporting

During the quarter ended December 31, 2014, there have been no changes in our internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15(d)-15(f) promulgated under the Securities Exchange Act of 1934, that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information
Other Information

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

On November 10, 2014, Akebia announced its financial results for the quarter ended September 30, 2014 and commented on certain corporate accomplishments and plans. The full text of the press release issued in connection

with the announcement is furnished as Exhibit 99.1 hereto.

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

PART III

Certain information required by Part III is omitted from this Annual Report on Form 10-K and is incorporated herein by reference from our definitive proxy statement relating to our 2015 Annual Meeting of Stockholders (the "Definitive Proxy Statement"), which we expect to file with the SEC no later than April 30, 2015.

Item 10. Director, Executive Officers and Corporate Governance

John P. Butler joined Akebia as director in July 2013 and was appointed as the President and Chief Executive Officer of Akebia in August 2013. Prior to joining Akebia, from 2011 until 2013, Mr. Butler served as the Chief Executive Officer of Inspiration Biopharmaceuticals, Inc., a biopharmaceutical company that filed for protection under Chapter 11 of the U.S. Bankruptcy Code in October 2012 prior to the successful sale of its hemophilia assets to Cangene Corporation and Baxter International in early 2013. From 1997 to 2011, Mr. Butler held various positions at Genzyme Corporation, a biopharmaceutical company, most recently serving as President of the company's rare genetic diseases business. From 2002 until 2010, Mr. Butler led Genzyme's renal division. Prior to his work at Genzyme, Mr. Butler held sales and marketing positions at Amgen and Hoffmann-La Roche. Mr. Butler currently serves as the chairman of board of trustees for the American Kidney Fund and a member of the board of directors of Relypsa, Inc. Mr. Butler received a B.A. in Chemistry from Manhattan College and an M.B.A. degree from Baruch College, City University of New York. We believe that Mr. Butler is qualified to serve on our board of directors due to his industry experience in the biotechnology sector, particularly his experience working in the renal disease market.

Jason A. Amello joined Akebia as Senior Vice President, Chief Financial Officer and Treasurer in 2013. Prior to joining Akebia, Mr. Amello served as Executive Vice President, Chief Financial Officer and Treasurer of ZIOPHARM Oncology, Inc., a biopharmaceutical company, from 2012 to 2013. From 2000 to 2011, Mr. Amello held various positions at Genzyme Corporation, most recently as Senior Vice President, Corporate Controller and Chief Accounting Officer. Earlier in his career, Mr. Amello spent 10 years in the business advisory and assurance practice of Deloitte, serving in various roles of increasing responsibility through senior manager. Mr. Amello holds a B.A. from Boston College and is a Certified Public Accountant in the Commonwealth of Massachusetts.

Brad Maroni, M.D. joined Akebia as Senior Vice President and Chief Medical Officer in August 2014. Prior to joining Akebia, Dr. Maroni served as Vice President, Medical Research at Biogen Idec from March 2012 to February 2014. Prior to that role, Dr. Maroni served as Chief Medical Officer of Stromedix, Inc. from June 2007 until the company was acquired by Biogen Idec in March 2012. His previous experience also includes serving as Executive Vice President and Chief Medical Officer at RenaMed Biologics, as well as multiple roles at Amgen Inc., including Vice President, Clinical Development and Anemia/Nephrology Therapeutic Area Head. At Amgen, Dr. Maroni led the cross-functional team responsible for the registration program and global regulatory approval of Aranesp®, a novel long-acting recombinant erythropoietic protein, indicated for the treatment of anemia in chronic kidney disease. During his tenure, Amgen also received approval for Sensipar®, a first-in-classsmall molecule for the treatment of bone disease in dialysis patients. Dr. Maroni trained as a nephrologist at Brigham and Women's Hospital in Boston, Massachusetts, after which he spent 10 years in academia at Emory University.

Nicole R. Hadas joined Akebia as Vice President, General Counsel and Secretary in 2013. Prior to joining Akebia, Ms. Hadas was Vice President and General Counsel at OvaScience, Inc., a biopharmaceutical company, in 2013. From 2011 to 2013, Ms. Hadas served as the Senior Vice President and General Counsel at Inspiration Biopharmaceuticals, Inc., a biopharmaceutical company that filed for protection under Chapter 11 of the U.S. Bankruptcy Code in October 2012, where she managed the successful sale of its hemophilia assets to Cangene Corporation and Baxter International in early 2013. From 2001 to 2011, Ms. Hadas worked at Genzyme Corporation, most recently as Senior Corporate Counsel. Prior to Genzyme, she was an associate at Foley Hoag representing biopharmaceutical companies and healthcare providers in a wide variety of matters. Ms. Hadas received a B.A. from the University of Michigan and a J.D. from Boston College Law School.

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

Item 11. Executive Compensation

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

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

The information required by this Item 12 will be contained in the Definitive Proxy Statement and is incorporated herein by reference.

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

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

Item 14. Principal Accountant Fees and Services

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

PART IV

Item 15. Exhibits and Financial Statement Schedules

Exhibits and Financial Statement Schedules

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

(1) Financial Statements

Report of Independent Registered Public Accounting Firm

Consolidated Balance Sheets

Consolidated Statements of Operations and Comprehensive Loss

Consolidated Statements of Stockholders' Equity (Deficit)

Consolidated Statements of Cash Flows

Notes to Consolidated Financial Statements

(2) Schedules

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

(3) Exhibits

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

SIGNATURES

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

AKEBIA THERAPEUTICS, INC.

Date: March 4, 2015

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

Date: March 4, 2015

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

Date: March 4, 2015

By: /s/ Muneer Satter
Muneer Satter
Chairman

Date: March 4, 2015

By: /s/ Anupam Dalal
Anupam Dalal
Director

Date: March 4, 2015

By: /s/ Jack Nielsen
Jack Nielsen
Director

Date: March 4, 2015

By: /s/ Duane Nash
Duane Nash
Director

Date: March 4, 2015

By: /s/ Michael Wyzga
Michael Wyzga
Director

By: /s/ Maxine Gowen

Date: March 4, 2015

Maxine Gowen
Director

Date: March 4, 2015 By: /s/ Michael Clayman
Michael Clayman
Director

Date: March 4, 2015 By: /s/ Ronald Renaud
Ronald Renaud
Director

EXHIBIT INDEX

Exhibit Number	Description of Exhibit
3.1	Ninth Amended and Restated Certificate of Incorporation (incorporated by reference to exhibit 3.1 to the Company's Current Report on Form 8-K, filed on March 28, 2014)
3.2	Amended and Restated Bylaws (incorporated by reference to exhibit 3.2 to the Company's Current Report on Form 8-K, filed on March 28, 2014)
4.1	Form of Common Stock Certificate (incorporated by reference to exhibit 4.1 to the Company's Registration Statement on Form S-1/A (333-193969), filed on March 4, 2014)
4.2	Third Amended and Restated Voting Agreement, dated May 10, 2013 (incorporated by reference to exhibit 4.2 to the Company's Registration Statement on Form S-1 (333-193969), filed on February 14, 2014)
4.3	Amendment No. 1 to the Third Amended and Restated Voting Agreement, dated May 31, 2013 (incorporated by reference to exhibit 4.3 to the Company's Registration Statement on Form S-1 (333-193969), filed on February 14, 2014)
4.4*	Fourth Amended and Restated Investors' Rights Agreement, dated March 5, 2014
10.1	Form of Director and Officer Indemnification Agreement (incorporated by reference to exhibit 10.1 to the Company's Registration Statement on Form S-1/A (333-193969), filed on March 4, 2014)
10.2	Office Lease Agreement Between MA-Riverview/245 First Street, L.L.C. and Akebia Therapeutics, Inc., dated December 3, 2013 (incorporated by reference to exhibit 10.2 to the Company's Registration Statement on Form S-1 (333-193969), filed on February 14, 2014)
10.3*	First Amendment to Office Lease Agreement Between Jamestown Premier 245 First, LLC and Akebia Therapeutics, Inc., dated December 15, 2014
10.4	Amended and Restated Administrative Services Agreement, between Akebia Therapeutics, Inc. and Aerpio Therapeutics, Inc., dated August 27, 2012 (incorporated by reference to exhibit 10.3 to the Company's Registration Statement on Form S-1 (333-193969), filed on February 14, 2014)
10.5	Administrative Services Agreement, between Akebia Therapeutics, Inc. and Aerpio Therapeutics, Inc., dated November 1, 2012 (incorporated by reference to exhibit 10.4 to the Company's Registration Statement on Form S-1 (333-193969), filed on February 14, 2014)
10.6†	Amended and Restated 2008 Equity Incentive Plan (incorporated by reference to exhibit 10.5 to the Company's Registration Statement on Form S-1 (333-193969), filed on February 14, 2014)

10.7†	Amendment No. 1 to Amended and Restated 2008 Equity Incentive Plan (incorporated by reference to exhibit 10.6 to the Company's Registration Statement on Form S-1 (333-193969), filed on February 14, 2014)
10.8†	Executive Employment Agreement with John P. Butler, dated September 16, 2013 (incorporated by reference to exhibit 10.7 to the Company's Registration Statement on Form S-1 (333-193969), filed on February 14, 2014)
10.9†	Executive Employment Agreement with Jason A. Amello, dated September 23, 2013 (incorporated by reference to exhibit 10.8 to the Company's Registration Statement on Form S-1 (333-193969), filed on February 14, 2014)
10.10†	Offer Letter to Nicole R. Hadas, dated November 13, 2013 (incorporated by reference to exhibit 10.9 to the Company's Registration Statement on Form S-1 (333-193969), filed on February 14, 2014)
10.11†	Executive Employment Agreement with Dr. Robert Shalwitz, dated April 6, 2011 (incorporated by reference to exhibit 10.10 to the Company's Registration Statement on Form S-1 (333-193969), filed on February 14, 2014)

10.12† Separation Agreement with Dr. Robert Shalwitz, dated August 5, 2014 (incorporated by reference to exhibit 10.1 to the Company's Quarterly Report on Form 10-Q, filed on November 10, 2014)

10.13† Consulting Agreement with Dr. Robert Shalwitz, dated August 5, 2014 (incorporated by reference to exhibit 10.2 to the Company's Quarterly Report on Form 10-Q, filed on November 10, 2014)

10.14† Amended and Restated Partial Recourse Promissory Note, dated May 9, 2013, with Robert Shalwitz (incorporated by reference to exhibit 10.20 to the Company's Registration Statement on Form S-1 (333-193969), filed on February 14, 2014)

10.15† Amended and Restated Partial Recourse Promissory Note, dated June 15, 2013, with Robert Shalwitz (incorporated by reference to exhibit 10.21 to the Company's Registration Statement on Form S-1 (333-193969), filed on February 14, 2014)

10.16† Forgiveness and Release Agreement, dated January 30, 2014, with Robert Shalwitz (incorporated by reference to exhibit 10.22 to the Company's Registration Statement on Form S-1 (333-193969), filed on February 14, 2014)

10.17†*Offer Letter with Bradley Maroni, M.D., dated July 21, 2014

10.18† 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)

10.19† 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)

10.20† Non-Employee Director Compensation Program (incorporated by reference to exhibit 10.26 to the Company's Registration Statement on Form S-1/A (333-193969), filed on March 4, 2014)

10.21† 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)

10.22† 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)

10.23† 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)

10.24† Cash Incentive Plan (incorporated by reference to exhibit 10.31 to the Company's Registration Statement on Form S-1/A (333-193969), filed on March 4, 2014)

10.25# Master Services Agreement by and between Evonik Corporation and Akebia Therapeutics, Inc., dated February 28, 2014 (incorporated by reference to exhibit 10.32 to the Company's Registration Statement on Form S-1/A (333-193969), filed on March 4, 2014)

10.26†*Form of Restricted Stock Unit Award Agreement under 2014 Incentive Plan

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 4, 2015 (furnished herewith)
101.INS*	XBRL Instance Document
101.SCH*	XBRL Taxonomy Extension Schema Document
101.CAL*	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	XBRL Taxonomy Extension Labels Linkbase Document
101.PRE*	XBRL Taxonomy Extension Presentation Linkbase Document

*Filed, or submitted electronically, herewith

†Indicates management contract or compensatory plan

#Indicates portions of the exhibit (indicated by asterisks) have been omitted pursuant to a request for confidential treatment

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