Akebia Therapeutics, Inc.
Form 424B4
March 21, 2014
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Filed Pursuant to Rule 424(b)(4)
Registration Nos. 333-193969 and 333-194695

PROSPECTUS

5,882,353 Shares

Akebia Therapeutics, Inc.

Common Stock

This is the initial public offering of shares of common stock of Akebia Therapeutics, Inc.

We are offering 5,882,353 shares of our common stock. Prior to this offering, there has been no public market for our common stock. Our common stock has been approved for listing on the NASDAQ Global Market under the trading symbol AKBA.

We are an emerging growth company under the federal securities laws and are subject to reduced public company reporting requirements.

Investing in our common stock involves a high degree of risk. See Risk Factors beginning on page 11.

	Per share	Total
Initial public offering price	$ 17.00	$ 100,000,001
Underwriting discounts and commissions(1)	$ 1.19	$ 7,000,000
Proceeds, before expenses, to Akebia	$ 15.81	$ 93,000,001

(1) See Underwriting for additional disclosure regarding underwriting discounts, commissions and expenses.

To the extent that the underwriters sell more than 5,882,353 shares of common stock, the underwriters have an option to purchase up to an additional 879,647 shares from us at the initial public offering price.

The underwriters expect to deliver the shares against payment in New York, New York on March 25, 2014.

Certain of our existing stockholders and their affiliated entities, including holders of more than 5% of our common stock, have agreed to purchase an aggregate of 887,929 shares of our common stock in this offering at the initial public offering price. The underwriters will receive the same underwriting discount on any shares purchased by these stockholders as they will on the shares sold to the public in this offering.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed on the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

Morgan Stanley **Credit Suisse**

UBS Investment Bank

Nomura

March 19, 2014

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We are responsible for the information contained in this prospectus and in any free-writing prospectus we prepare or authorize. We have not, and the underwriters have not, authorized anyone to provide you with different information, and we take no responsibility for any other information others may give you. We are not, and the underwriters are not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should not assume that the information contained in this prospectus is accurate as of any date other than the date on the cover page of this prospectus.

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Summary

This summary highlights information contained in other parts of this prospectus and does not contain all of the information that you should consider in making your investment decision. Before investing in our common stock, you should carefully read this entire prospectus, including our financial statements and the related notes and the information set forth under the sections titled Risk Factors, Cautionary Note Regarding Forward-Looking Statements and Management s Discussion and Analysis of Financial Condition and Results of Operations. Unless the context requires otherwise, references in this prospectus to Akebia, we, us, our, the Company and similar designations refer to Akebia Therapeutics, Inc.

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. Our lead product candidate, AKB-6548, is being developed as a once-daily oral therapy that has successfully completed a Phase 2a proof of concept study demonstrating that AKB-6548 safely and predictably raised hemoglobin levels in patients with anemia secondary to chronic kidney disease, or CKD, not requiring dialysis.

We are conducting a Phase 2b trial for AKB-6548 in patients with anemia secondary to CKD who are not dependent on dialysis and expect data to be available in the fourth quarter of 2014. We have also initiated a development program for patients dependent on dialysis. If the results of our Phase 2b trial are positive, we would expect to initiate Phase 3 trials for anemia secondary to CKD in 2015, and would anticipate submitting a New Drug Application, or NDA, for AKB-6548 in the United States by 2018 if the Phase 3 data are favorable.

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 eight clinical trials across four separate patient populations: healthy volunteers and patients with CKD stages 3, 4 and 5 (non-dialysis). Our largest study was a Phase 2a trial in 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.

Our ongoing Phase 2b trial explores a dosing approach for AKB-6548 to enable subjects with anemia secondary to CKD to appropriately and safely raise hemoglobin levels. As of February 28, 2014, we had enrolled over 80% of our targeted 200 patients in this study at investigational sites in the United States, with data expected in the fourth quarter of 2014. With positive data, we plan to progress to Phase 3 global registration studies for AKB-6548 in patients with anemia secondary to CKD. We anticipate the design of the Phase 3 studies will mirror the Phase 2b study, except that they will be longer and larger in size, positioning us to file for approval in the United States by 2018.

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 of 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, including idiopathic anemia of aging, or IAA, and anemia of congestive heart failure.

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 Corp. s renal division which grew to over $1 billion in annual revenue under his leadership, and is current 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 executive team also includes Robert Shalwitz, M.D., CMO and co-founder of Akebia. Dr. Shalwitz is an academic pediatric endocrinologist and has extensive industry experience developing novel pharmaceuticals at Abbott Laboratories and Reliant Pharmaceuticals. He has developed extensive knowledge of HIF biology over his career, particularly over the past seven years in leading development at Akebia.

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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 plan to complete the Phase 2b trial that is currently enrolling in the United States. 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 would anticipate submitting an NDA for AKB-6548 in the United States by 2018 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.

Continue to develop AKB-6548 for further indications. We plan to initiate, in the first half of 2014, a Phase 2 study for AKB-6548 in dialysis patients with anemia, the second indication we intend to pursue. Additionally, we plan to evaluate the product candidate in IAA and other indications.

Advance our earlier stage pipeline asset. 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 Phase 1 trials to determine its potential use in oncology and ophthalmology.

Acquire or in-license additional nephrology products. If we are able to successfully launch AKB-6548, we will look to leverage our commercial infrastructure with additional products that would be prescribed by nephrologists.

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

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. We expect AKB-6548 to 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.

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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 in the treatment of anemia secondary to CKD.

AKB-6548 significantly increases hemoglobin in anemic CKD patients. We have successfully completed a Phase 2a trial, in which AKB-6548 significantly increased hemoglobin levels compared to baseline in a dose-dependent manner across all treatment arms ($p < 0.0001$). 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, meaning that these improvements occur without causing patients hemoglobin to rise 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.

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, such as idiopathic anemia of aging. 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 a dose-related increase in 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 2a study, no drug-related serious adverse events were reported. Dosing was well-tolerated and there was no evidence of undesirable vascular response.

Risk Associated with Our Business

An investment in our common stock involves a high degree of risk. Any of the factors set forth under Risk Factors may limit our ability to successfully execute our business strategy. You should carefully consider all of the information set forth in this prospectus and, in particular, should evaluate the specific factors set forth under Risk Factors in deciding whether to invest in our common stock. These risk factors include, among others:

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

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 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.

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

Clinical drug development is a lengthy and expensive process with an uncertain outcome, and positive results from Phase 1 and Phase 2a clinical trials of AKB-6548 are not necessarily predictive of the results of our current Phase 2b and any future clinical trials of AKB-6548. If we cannot replicate the positive results from our Phase 1 and Phase 2a clinical trials of AKB-6548 in our Phase 2b and subsequent clinical trials, we may be unable to successfully develop, obtain regulatory approval for and commercialize AKB-6548.

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.

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.

Third-party claims of intellectual property infringement may be costly and time consuming, and may delay or harm our drug discovery and development efforts. We are currently involved in an opposition proceeding involving the granted European patent of one of our potential competitors.

Implications of Being an Emerging Growth Company

As a company with less than $1 billion in revenue during our most recently completed fiscal year, we qualify as an emerging growth company as defined in Section 2(a) of the Securities Act of 1933, as amended, or the Securities Act, as modified by the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. As an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable, in general, to public companies that are not emerging growth companies. These provisions include:

Reduced disclosure about our executive compensation arrangements;

Exemption from the non-binding shareholder advisory votes on executive compensation or golden parachute arrangements;

Exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting; and

Reduced disclosure of financial information in this prospectus, such as being permitted to include only two years of audited financial information and two years of selected financial information in addition to any required unaudited interim financial statements, with correspondingly reduced Management s Discussion and Analysis of Financial Condition and Results of Operations disclosure.

We may take advantage of these exemptions for up to five years or such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company if we have more than $1 billion in annual revenues as of the end of a fiscal year, have more than $700 million in market value of our capital stock held by non-affiliates as of any June 30 or if we issue more than $1 billion of non-convertible

debt over a three-year-period. We may choose to take advantage of some, but not all, of the available exemptions. We have

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taken advantage of some reduced reporting burdens in this prospectus. Accordingly, the information contained herein may be different than the information you receive from other public companies in which you hold stock.

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 have irrevocably elected not to avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for non-emerging growth companies.

Corporate Information

We were incorporated under the laws of the state of Delaware in February 2007. In December 2011, we spun out our programs focused on the treatment of diabetic eye disease and inflammatory bowel disease into Aerpio Therapeutics, Inc., or Aerpio, which has since operated as a stand-alone company. Our principal executive office is located at 245 First Street, Suite 1100, Cambridge MA 02142, and our telephone number is 617-871-2098. Our website address is *www.akebia.com*. We have included our website address in this prospectus solely as an inactive textual reference. The information on, or that can be accessed through, our website is not part of this prospectus, and you should not rely on any such information in making the decision whether to purchase our common stock.

This prospectus contains trademarks and tradenames of other businesses that are the property of their respective owners. We have omitted the ® and ™ designations, as applicable, for the trademarks named in this prospectus.

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The Offering

Common stock offered by us	5,882,353 shares
Common stock to be outstanding immediately following this offering	19,268,027 shares
Underwriters over-allotment option	The underwriters have an option to purchase up to 879,647 additional shares of common stock to cover over-allotments as described in Underwriting.
Use of proceeds	The net proceeds from the issuance of our common stock in this offering will be approximately $90.2 million, or approximately $104.1 million if the underwriters exercise their over-allotment option in full, after deducting underwriting discounts and commissions and estimated offering expenses payable by us. We intend to use the net proceeds from this offering to continue clinical development of AKB-6548 in patients with anemia secondary to CKD, including the preparation for and initiation of the Phase 3 trials; to conduct a Phase 2 clinical trial of AKB-6548 in idiopathic anemia of aging; to advance our preclinical candidate, AKB-6899, through Phase 1 development in oncology; and for working capital and other general corporate purposes. See Use of Proceeds for additional information.
Risk factors	See Risk Factors and the other information included in this prospectus for a discussion of factors you should carefully consider before deciding to invest in our common stock.
NASDAQ Global Market symbol	Our common stock has been approved for listing on the NASDAQ Global Market under the symbol AKBA.

Certain of our existing stockholders and their affiliated entities, including holders of more than 5% of our common stock, have agreed to purchase an aggregate of 887,929 shares of our common stock in this offering at the initial public offering price.

The number of shares of common stock to be outstanding after this offering is based on 13,385,674 shares of common stock outstanding as of December 31, 2013, including 957,189 shares of restricted stock and 12,002,329 shares of our common stock issuable upon the conversion of all outstanding shares of our preferred stock, and excludes the following:

- 1,251,398 shares of common stock issuable upon exercise of stock options outstanding as of December 31, 2013 at a weighted-average exercise price of $1.01 per share;
- 155,108 shares of common stock reserved for future issuance under our Amended and Restated 2008 Equity Incentive Plan as of December 31, 2013;
- 1,785,000 shares of common stock reserved for future issuance under our 2014 Incentive Plan; and

112,853 shares of common stock issuable upon conversion of our Series C preferred stock with respect to dividends accrued between December 31, 2013 and the consummation of the offering.

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Unless otherwise indicated, all information in this prospectus reflects or assumes the following:

- a 1.75-for-1 forward stock split of our common stock that we effected on March 6, 2014;
- the amendment and restatement of our certificate of incorporation and bylaws, which will occur immediately prior to the closing of this offering;
- the conversion of all of our outstanding shares of preferred stock into 12,002,329 shares of common stock, which is calculated based upon accrued dividends through December 31, 2013 and excludes 112,853 shares of common stock issuable upon conversion of our Series C preferred stock at the closing of this offering with respect to dividends accrued between December 31, 2013 and the consummation of the offering;
- no grants, exercises or forfeitures of stock options or restricted stock on or after December 31, 2013; and
- no exercise by the underwriters of their option to purchase up to an additional 879,647 shares of common stock in this offering.

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Summary Financial Data

The following summary financial data for the years ended December 31, 2012 and 2013, and the period from February 27, 2007 (inception) to December 31, 2013 are derived from our audited financial statements included elsewhere in this prospectus. You should read this data together with our financial statements and related notes included elsewhere in this prospectus and the information under the captions Selected Financial 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,		Period from February 27, 2007 (Date of Inception) to December 31,
	2012	2013	2013
	(dollars in thousands, except per share data)		
Consolidated statements of operations data:			
Revenue		$	$
Expenses:			
Research and development	5,632	10,781	51,748
General and administrative	2,891	5,152	15,269
Total expenses	8,523	15,933	67,017
Loss from operations	(8,523)	(15,933)	(67,017)
Other income, net	327	2,766	3,975
Net loss	$ (8,196)	$ (13,167)	$ (63,042)
Net loss per share applicable to common stockholders basic and diluted[1]	$ (27.82)	$ (126.94)	$ (481.04)
Weighted-average number of common shares used in net loss per share applicable to common stockholders basic and diluted		544,002	
Pro forma net loss per share applicable to common stockholders basic and diluted (unaudited)[1]		$ (1.31)	
Pro forma weighted-average number of common shares used in net loss per share applicable to common stockholders basic and diluted (unaudited)		10,132,528	

(1) See Note 2 within the notes to our financial statements appearing elsewhere in this prospectus for a description of the method used to calculate basic and diluted net loss per share of common stock. Pro forma basic and diluted net loss per share of common stock is calculated by dividing net loss attributable to common stockholders, excluding the impact of gains (losses) on the extinguishment of preferred stock, accretion of preferred stock and including the impact of compensation expense associated with awards of restricted stock that contain a performance condition wherein vesting is contingent upon our consumption of a Liquidity Event, as defined in the Restricted Stock Agreement from the December 23, 2013 grants, by the pro forma weighted-average number of common shares outstanding.

The pro forma balance sheet data set forth below give effect to an assumed conversion as of December 31, 2013 of all outstanding shares of our preferred stock into an aggregate of 12,002,329 shares of our common stock, which does not include an additional 112,853 shares issuable upon such conversion with respect to dividends on our Series C preferred stock between December 31, 2013 and the consummation of the offering, at which time all shares of our preferred stock will automatically convert into common stock.

The pro forma as adjusted balance sheet data set forth below give further effect to our issuance and sale of 5,882,353 shares of our common stock in this offering at the initial public offering price of $17.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

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	As of December 31, 2013		
	Actual	Pro forma (in thousands)	Pro forma as adjusted
Balance Sheet Data:			
Cash and cash equivalents	$ 21,215	$ 21,215	$ 111,411
Working capital	29,529	29,529	119,725
Total assets	34,665	34,665	124,861
Redeemable convertible preferred stock	157,827		
Deficit accumulated during the development stage	(127,072)	(63,707)	(63,707)
Total stockholders (deficit) equity	(127,072)	30,755	120,951

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Risk Factors

Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below together with all of the other information contained in this prospectus, including our financial statements and the related notes appearing at the end of this prospectus, before deciding to invest in our common stock. If any of the following risks actually occur, our business, prospects, operating results and financial condition could suffer materially, the trading price of our common stock could decline and you could lose all or part of your investment. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently believe to be immaterial may also adversely affect our business.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred 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 $8.2 million for the year ended December 31, 2012, and $13.2 million for the year ended December 31, 2013. As of December 31, 2013, we had an accumulated deficit of $127.1 million. To date, we have not commercialized any products or generated any revenues from the sale of products, and we do not expect to generate any product revenues 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 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, is currently in an ongoing Phase 2b clinical trial, and our other product candidate is in preclinical development. As a result, 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 revenues will depend upon the size of any markets in which AKB-6548 has received approval, our ability to achieve sufficient market acceptance, reimbursement from third-party payors and other factors.

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

- continue our Phase 2b trial and prepare for a future 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 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 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

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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 EMA or other regulatory authorities to perform studies in addition to 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 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 revenues that are 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 you to lose all or part of your 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, 2013, our cash and cash equivalents were $21.2 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, results and cost of completing our Phase 2b clinical trial of AKB-6548 and our operating costs incurred as we conduct these trials and through our end of Phase 2 meeting with the FDA, and equivalent meetings with the EMA and other regulatory authorities;

assuming AKB-6548 advances to Phase 3 clinical trials, the scope, size, rate of progress, results and costs of initiating and completing our Phase 3 development program of AKB-6548;

assuming favorable 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 preclinical development, laboratory testing and clinical trials for AKB-6899 and any other product candidates that we may develop or acquire;

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- the timing of, and the costs involved in, obtaining regulatory approvals for AKB-6899 if clinical trials 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 in preparation for regulatory approval 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, prosecuting patent applications, 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 receive from this offering, and our existing cash and cash equivalents and investments 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 revenues, 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, your ownership interest will be diluted, and the terms may include liquidation or other preferences and anti-dilution protections that adversely affect your rights as a stockholder. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take certain actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through strategic 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.

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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 fraction 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 drug 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. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

In addition, as a 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 is in a Phase 2b clinical trial. Even if we obtain favorable clinical results, 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 revenues from sales of any drugs, and may never be able to develop marketable drug products. AKB-6548, which is currently in an ongoing Phase 2b clinical trial, 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 such study is initiated, if ever. 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 of an NDA from the FDA, or in any foreign countries until we receive the requisite approval from such countries. As a condition to submitting an NDA to the FDA for AKB-6548 regarding its ability to treat patients with anemia secondary to CKD, we must complete our ongoing Phase 2b clinical trial, Phase 3 studies, and any additional non-clinical or clinical studies required by the FDA. To date, we have only commenced the Phase 2b clinical trial. 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

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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 of AKB-6548;
- the FDA may require that we conduct additional clinical trials;
- the contract research organizations, or CROs, that we retain to conduct our clinical trials may 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 our interpretation of data from our preclinical studies and clinical trials;
- the FDA may not approve the manufacturing processes or facilities of third-party manufacturers with which 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 our product candidates.

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

As we have not completed our Phase 2b clinical trial, 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 upon successful completion of our Phase 2b clinical trial. If the FDA determines that the Phase 2b trial 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 our proposed design of our Phase 3 development program and could

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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 application.

We have not yet sought guidance for the regulatory path for AKB-6548 with 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 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 trials for AKB-6548 because of negative publicity from adverse events observed in 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 current injectable rESAs may be reluctant to participate in a clinical trial with an investigational drug. 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.

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We may not be able to comply with requirements of foreign jurisdictions in conducting trials outside of the United States. In addition, we may not be able to obtain regulatory approval in foreign jurisdictions.

We currently expect to seek regulatory approval for 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 foreign country, 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 and physicians;
- different local standards for the conduct of clinical studies;
- the potential burden of complying with a variety of foreign laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatments; and
- the acceptability of data obtained from studies conducted in the United States to the EMA and other regulatory authorities.

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 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 foreign regulatory authority does not ensure approval by regulatory authorities in other foreign 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 foreign regulatory approval process may include all of the risks associated with obtaining FDA approval. We may not obtain foreign regulatory approvals on a timely basis, if at all. We may not be able to file for regulatory approvals and may not receive necessary approvals to commercialize our drug products in any market.

Clinical drug development is a lengthy and expensive process with an uncertain outcome, and positive results from Phase 1 and Phase 2a clinical trials of AKB-6548 are not necessarily predictive of the results of our current Phase 2b and any future clinical trials of AKB-6548. If we cannot replicate the positive results from our Phase 1 and Phase 2a clinical trials of AKB-6548 in our Phase 2b and subsequent 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 early encouraging preclinical and clinical results for AKB-6548 do not ensure that the results of our ongoing Phase 2b clinical trial or any future clinical trials will demonstrate similar results. Our current Phase 2b clinical trial and 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

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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 2b clinical trial for AKB-6548 and we do not know whether 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 or trial site 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 revenues. 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 to conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, 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, registration, 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;

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fines, warning letters or holds on clinical trials;

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 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 studies and clinical trials for our product candidates, and if they do not properly and successfully perform their obligations to us, we may not be able to obtain regulatory approvals for our product candidates.

We rely on third party CROs and other third parties to assist in managing, monitoring and otherwise carrying out our ongoing Phase 2b trial of AKB-6548. 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 at any time, 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 foreign regulatory authorities 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 trial participants 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 under 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 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 produced 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.

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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, producing 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 conduct our product candidate manufacturing for research and preclinical and clinical testing. We currently rely, and expect to rely, on third parties to manufacture and supply drug products for our AKB-6548 clinical trials, and we expect to continue to rely on third parties for the manufacture of clinical and, if necessary, 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.

Any of these third parties may terminate their engagement with us at any time. We believe we have sufficient drug product to complete our ongoing Phase 2b trial of AKB-6548. On February 28, 2014, we entered into an agreement with Evonik Corporation, or Evonik, for the manufacturing of the drug substance for the Phase 3 development program of AKB-6548. If Evonik cannot perform as agreed, we may be required to find replacement manufacturers. We also do not currently have arrangements in place for the manufacturing of drug product for the Phase 3 development program. Although we believe that there are several potential alternative manufacturers who could manufacture our product candidates, we may incur significant delays and added costs in identifying, qualifying and contracting with any such replacement, as well as producing the drug product. In addition, we have to enter into technical transfer agreements and share our know-how with the 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 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

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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 supplies 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 due to non-compete 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, 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, or development of, facilities to manufacture our product candidates at sufficient yields and at 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 product on a commercial scale, replacement of a manufacturer may be expensive and time-consuming and may cause interruptions in the production of our drug product. 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;

shortages of qualified personnel;

compliance with strictly enforced federal, state and foreign 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 could have a material adverse effect on our business, financial condition, results of operations and cash flows.

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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 unpartnered 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 our market.

In July of 2011, a third party filed an opposition to one of our issued European patents, European Patent No. 2044005, which we refer to as 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 lead 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.

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This type of 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 foreign countries. Even if the 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 USPTO, 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 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 foreign 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 our 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 and develop and to 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 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 in the future 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. We are currently involved in an opposition proceeding involving the granted European patent of one of our potential competitors.

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 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, Inc., or FibroGen, directed to certain heterocyclic carboxamide compounds that are described as inhibitors of prolyl-4-hydroxylase. Those patents, however, expire as of December 2014, absent extension, before we anticipate receiving regulatory approval for our product candidates. 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

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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 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. 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. Notwithstanding the above, third parties, including FibroGen, may in the future claim that our product candidates and other technologies infringe upon these patents and may file suit against us.

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

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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 proceedings and may in the future be involved in lawsuits or administrative proceedings 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. These proceedings may be ongoing for a number of years and may involve substantial expense and diversion of employee resources from our business. 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 USPTO or oppositions and other comparable proceedings in foreign jurisdictions. Interference proceedings provoked by third parties or brought by the USPTO 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 USPTO 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 USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO 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 noncompliance 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

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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 product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can 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 foreign countries 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.

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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 label approved by regulatory authorities for use with the product, including any warnings that may be required on the label;
- acceptance by physicians and patients of the product as a safe and effective treatment 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 treatment 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 and Fresenius, account for more than half of the injectable rESA sales in the U.S. dialysis market and have entered into long-term sales agreements with Amgen 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.

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 have no experience in the sale, marketing or distribution of pharmaceutical 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.

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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 physicians or persuade adequate numbers of physicians to prescribe any future products;
- our inability to effectively manage 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 an independent 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 is available only to limited levels, we may not be able to commercialize certain of our products. In addition, in the United States third-party 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 reimburse patients for their use of 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

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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 treatment 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 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, the 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,

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

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

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 foreign governments 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 the 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 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 outside of the United States. 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 it is approved and launched commercially. These candidates are being developed by such companies as FibroGen/AstraZeneca, Japan Tobacco, GlaxoSmithKline and Bayer. FibroGen, 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.

Since rESAs are biologic products, the introduction of biosimilars into the rEPO 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

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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, a version of rEPO, 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 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.

Many of our potential competitors have significantly greater financial, manufacturing, marketing, drug development, technical and human resources than we do. Large pharmaceutical companies, in particular, have extensive experience in clinical testing, obtaining regulatory approvals, recruiting patients and in manufacturing pharmaceutical products. 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 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 products liability claims. We are currently conducting a Phase 2b clinical trial for AKB-6548. Serious adverse events deemed to be caused by our product candidates could have a material adverse effect on the development of our product candidates and our business as a whole. The most common drug-related adverse events to date in the clinical trial evaluating the safety and tolerability of AKB-6548 have been gastro-intestinal disorders. Our understanding of the relationship between AKB-6548 and these events, as well as 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.

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.

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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.

We are highly dependent on members of our senior management, including John Butler, our President and Chief Executive Officer and Robert Shalwitz, our Chief Medical Officer. The loss of the services of either of these persons could impede the achievement of our research, development and commercialization objectives.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be critical to our success. 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, including Dr. Shalwitz, our Chief Medical Officer, 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. For example, Dr. Shalwitz is expected to spend approximately 5% of his time providing services to Aerpio. 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 noncompliance 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) manufacturing standards, (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. 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 other 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

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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 management, administrative and, if necessary, sales and marketing personnel. We may not be able to accomplish these tasks, and our failure to accomplish any of them could prevent us from successfully growing our company.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our 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 a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our 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 trial participants or patients;

product recalls, 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

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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 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 our use of hazardous materials, 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 requirements to apply for or to otherwise be eligible to receive certain contracts or grants 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 awardee. Even if we are able to satisfy the award requirements, there is no guarantee that we will be a successful awardee. 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 and This Offering

We are eligible to be treated as an emerging growth company as defined in the Jumpstart Our Business Startups Act of 2012, and we cannot be certain if the reduced disclosure requirements applicable to emerging growth companies will make our common stock less attractive to investors.

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:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced Management s Discussion and Analysis of Financial Condition and Results of Operations disclosure;

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not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;

not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board;

reduced disclosure obligations regarding executive compensation; and

exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

We have taken advantage of reduced reporting burdens in this prospectus. In particular, in this prospectus, we have provided only two years of audited financial statements and have not included all of the executive compensation related information that would be required if we were not an emerging growth company. 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, 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 June 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. Even after we no longer qualify as an emerging growth company, we may still qualify as a smaller reporting company if the market value of our common stock held by non-affiliates is below $75 million as of June 30 in any given year, which would allow us to take advantage of many of the same exemptions from disclosure requirements, including exemption from the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements.

We do not know whether a market will develop for our common stock or what the market price of our common stock will be and, as a result, it may be difficult for you to sell your shares of our common stock.

Before this offering, there was no public trading market for our common stock. If a market for our common stock does not develop or is not sustained, it may be difficult for you to sell your shares of common stock at an attractive price, or at all. Further, an inactive market may also impair our ability to raise capital by selling shares of our common stock and may impair our ability to enter into strategic collaborators or acquire companies or products by using our shares of common stock as consideration. We cannot predict the prices at which our common stock will trade. It is possible that in one or more future periods our results of operations may be below the expectations of public market analysts and investors and, as a result of these and other factors, the price of our common stock may fall.

Certain of our existing stockholders and their affiliated entities, including holders of more than 5% of our common stock, have agreed to purchase an aggregate of 887,929 shares of our common stock in this offering at the initial public offering price. Such purchases may reduce the available public float for our shares because certain of these stockholders will be restricted from selling the shares by restrictions under applicable securities laws and lock-up agreements described in the Shares Eligible for Future Sale section of this prospectus. As a result, the

liquidity of our common stock could be significantly reduced from what it would have been if these shares had not been purchased by investors that were not affiliated with us.

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

The initial public offering price for our shares will be determined by negotiations between us and the representatives of the underwriters and may not be indicative of prices that will prevail in the trading market. The market price of shares of our common stock could be subject to wide fluctuations in response to many risk factors listed in this section, and others beyond our control, including:

- results of clinical trials of our product candidates;
- the timing of the release of results of our clinical trials;
- results of clinical trials of our competitors products;
- safety issues with respect to our products or our competitors products;
- regulatory actions with respect to our products or our competitors products;
- actual or anticipated fluctuations in our financial condition and operating results;
- publication of research reports by securities analysts about us or our competitors or our industry;
- our failure or the failure of our competitors to meet analysts projections or guidance that we or our competitors may give to the market;
- additions and departures of key personnel;
- strategic decisions by us or our competitors, such as acquisitions, divestitures, spin-offs, joint ventures, strategic investments or changes in business strategy;
- the passage of legislation or other regulatory developments affecting us or our industry;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- sales of our common stock by us, our insiders or our other stockholders;
- speculation in the press or investment community;

announcement or expectation of additional financing efforts;

changes in accounting principles;

terrorist acts, acts of war or periods of widespread civil unrest;

natural disasters and other calamities;

changes in market conditions for biopharmaceutical stocks; and

changes in general market and economic conditions.

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

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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.

As of December 31, 2013, our executive officers, directors and principal stockholders, together with their respective affiliates, owned approximately 80% of our common stock, including shares subject to outstanding options that are exercisable within 60 days after such date, and we expect that upon completion of this offering that same group will continue to hold at least 70% of our outstanding common stock. Accordingly, even after this offering, 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.

A significant portion of our total outstanding shares may be sold into the public market in the near future, which could cause the market price of our common stock to drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time after the expiration of the lock-up agreements described in the Underwriting section of this prospectus. These sales, or the market perception that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. After this offering, we will have 19,383,045 shares of common stock outstanding (including the 112,853 shares of common stock that will be issued upon conversion of the Series C preferred stock with respect to dividends accrued between December 31, 2013 and the closing of the offering, as well as ordinary course activity under the Company s equity incentive plans). This includes the 5,882,353 shares that we are selling in this offering, which may be resold in the public market immediately subject to any restrictions imposed on our affiliates under Rule 144 or lock-up agreements. The remaining shares, or 13,500,692 of our outstanding shares after this offering, are currently restricted as a result of securities laws or lock-up agreements but will be able to be sold, subject to any applicable volume limitations under federal securities laws with respect to affiliate sales, in the near future as set forth below.

In addition, as of December 31, 2013, there were 1,251,398 shares subject to outstanding options that will become eligible for sale in the public market to the extent permitted by any applicable vesting requirements, the lock-up agreements and Rules 144 and 701 under the Securities Act. Moreover, after this offering, holders of an aggregate of 13,171,517 shares of our common stock will have rights, subject to some conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. If such holders, by exercising their registration rights, cause a large number of securities to be registered and sold into the public market, these sales could have an adverse effect on the market price for our common stock. We also intend to register all shares of common stock that we may issue under our employee benefit plans, including our 2014 Incentive Plan. Once we register these shares and they are issued in accordance with the terms of the plans, they can be freely sold in the public market upon issuance, subject to the lock-up agreements and the restrictions imposed on our affiliates under Rule 144. For more information, see Shares Eligible for Future Sale Rule 144 .

You will incur immediate and substantial dilution as a result of this offering.

The initial public offering price of our common stock will be substantially higher than the net tangible book value per share of our common stock. Therefore, if you purchase common stock in this offering, you will pay a price per share that substantially exceeds our pro forma adjusted net tangible book value per share after this offering. To the extent shares subsequently are issued under options, you will incur further dilution. Based on the initial public offering price of $17.00, you will incur immediate and substantial dilution of $10.72 per share, representing the difference between our pro forma net tangible book value per share, after giving effect to this offering, and the initial public offering price. In addition, purchasers of common stock in this offering will have contributed approximately 51.9% of the aggregate price paid by all purchasers of our stock but will own approximately 30.5% of our common stock outstanding after this offering.

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We have broad discretion in the use of net proceeds from this offering and may not use them effectively.

We currently intend to use the net proceeds from this offering for continuing clinical development of AKB-6548 in patients with anemia secondary to CKD, including the preparation for and initiation of the Phase 3 trials, for conducting a Phase 2 clinical trial of AKB-6548 in idiopathic anemia of aging, or IAA, for advancing AKB-6899 through Phase 1 development in oncology and for working capital and other general corporate purposes. See the section of this prospectus entitled Use of Proceeds. Although we currently intend to use the net proceeds from this offering in such a manner, we will have broad discretion in the application of the net proceeds. Our failure to apply these funds effectively could affect our ability to continue to develop and commercialize our product candidates. Pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or loses value.

We will incur increased costs as a result of being a public company and our management expects to devote substantial time to public company compliance programs.

As a public company, we will incur significant legal, insurance, accounting and other expenses that we did not incur as a private company. In addition, our administrative staff will be required to perform additional tasks. We intend to invest resources to comply with evolving laws, regulations and standards, and this investment will result in increased general and administrative expenses and may divert management s time and attention from product development activities. If our efforts to comply with new laws, regulations and standards differ from the activities intended by regulatory or governing bodies due to ambiguities related to practice, regulatory authorities may initiate legal proceedings against us and our business may be harmed. In connection with this offering, we are increasing our directors and officers insurance coverage, which will increase our insurance cost. In the future, it will be more expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced coverage or incur substantially higher costs to obtain coverage. These factors could also make it more difficult for us to attract and retain qualified members of our board of directors, particularly to serve on our audit committee and compensation committee, and qualified executive officers.

In addition, in order to comply with the requirements of being a public company, we may need to undertake various actions, including implementing new internal controls and procedures and hiring new accounting or internal audit staff. The Sarbanes-Oxley Act requires that we maintain effective disclosure controls and procedures and internal control over financial reporting. We are continuing to develop and refine our disclosure controls and other procedures that are designed to ensure that information required to be disclosed by us in the reports that we file with the SEC is recorded, processed, summarized and reported within the time periods specified in the SEC s rules and forms, and that information required to be disclosed in reports under the Securities Exchange Act of 1934 as amended, or the Exchange Act, is accumulated and communicated to our principal executive and financial officers. Any failure to develop or maintain effective controls could adversely affect the results of periodic management evaluations. In the event that we are not able to demonstrate compliance with the Sarbanes-Oxley Act, that our internal control over financial reporting is perceived as inadequate, or that we are unable to produce timely or accurate financial statements, investors may lose confidence in our operating results and the price of our ordinary shares could decline. In addition, if we are unable to continue to meet these requirements, we may not be able to remain listed on NASDAQ.

We are not currently required to comply with the SEC s rules that implement Section 404 of the Sarbanes-Oxley Act, and are therefore not yet required to make a formal assessment of the effectiveness of our internal control over financial reporting for that purpose. Upon becoming a public company, we will be required to comply with certain of these rules, which will require management to certify financial and other information in our quarterly and annual reports and provide an annual management report on the effectiveness of our internal control over financial reporting commencing with our second annual report. This assessment will need to include the disclosure of any material weaknesses in our internal control over financial reporting identified by our management or our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate

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internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statement.

Our independent registered public accounting firm will not be required to formally attest to the effectiveness of our internal control over financial reporting until the later of our second annual report or the first annual report required to be filed with the SEC following the date we are no longer an emerging growth company as defined in the JOBS Act. We cannot assure you that there will not be material weaknesses or significant deficiencies in our internal controls in the future.

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 that will become effective upon the closing of this offering 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 certificate of incorporation.

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

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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 if we undergo an ownership change in connection with or after this offering, our ability to utilize NOLs could be further limited by Section 382 of the Code. In addition, 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 that will become effective upon the closing of this offering 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 in respect of, one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions, which could adversely affect our business and financial condition.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain.

You should not rely on an investment in our common stock to provide dividend income. We do not anticipate that we will pay any cash dividends to holders of our common stock in the foreseeable future. Instead, we plan to

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retain any earnings to maintain and expand our operations. In addition, any future debt financing arrangement may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. Accordingly, investors must rely on sales of their common stock after price appreciation, which may never occur, as the only way to realize any return on their investment. As a result, investors seeking cash dividends should not purchase our common stock.

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Cautionary Note Regarding Forward-Looking Statements

This prospectus contains forward-looking statements. These statements include all matters that are not related to present facts or current conditions or that are not historical facts, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, objectives of management and expected market growth. The words anticipate, believe, could, estimate, expe intend, may, plan, will, would, or the negative of these terms or other similar expressions are intended to identify forward-looking statement although not all forward-looking statements contain these identifying words.

The forward-looking statements in this prospectus include, among other things, statements about:

- the timing of data from our pending Phase 2b trial of AKB-6548, the timing of commencement of our Phase 3 development program of AKB-6548 and the timing of our submission of an NDA for AKB-6548;
- 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 commercialization, marketing and manufacturing capabilities and strategy;
- the rate and degree of market acceptance and clinical utility of our products;
- our competitive position;
- our intellectual property position;
- developments and projections relating to our competitors and our industry;
- our ability to establish collaborations or obtain additional funding;
- our expectations regarding the time during which we will be an emerging growth company under the JOBS Act;

our expectations related to the use of proceeds from this offering; and

our estimates regarding expenses, future revenue, capital requirements and needs for additional financing.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this prospectus, particularly in the Risk Factors section, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

You should read this prospectus and the documents that we reference in this prospectus and have filed as exhibits to the registration statement of which this prospectus is a part completely and with the understanding that our actual future results may be materially different from what we expect. The forward-looking statements in this prospectus represent our views as of the date of this prospectus. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking

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statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this prospectus.

Industry and Market Data

This prospectus includes statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties. Industry publications and third party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information.

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Use of Proceeds

The net proceeds from the sale of 5,882,353 shares of common stock in this offering will be approximately $90.2 million after deducting underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their option to purchase additional shares in full, the net proceeds will be approximately $104.1 million after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

We intend to use the net proceeds from this offering as follows:

- approximately $50.0 million to continue clinical development of AKB-6548 in patients with anemia secondary to CKD, including the preparation for and initiation of the Phase 3 trials;
- approximately $10.0 million to conduct a Phase 2 clinical trial of AKB-6548 in idiopathic anemia of aging;
- approximately $5.0 million to advance our preclinical candidate, AKB-6899, through Phase 1 development in oncology; and
- the remainder for working capital and other general corporate purposes.

Our expected use of net proceeds from this offering represents our intentions based upon our present plans and business conditions, which could change in the future as our plans and business conditions evolve. The amount and timing of our actual expenditures will depend upon numerous factors, including the results of our research and development efforts, the timing and success of preclinical studies, our ongoing clinical studies or clinical studies we may commence in the future, the timing of regulatory submissions and the feedback from regulatory authorities. As a result, our management will have broad discretion over the use of the net proceeds from this offering.

Pending the use of the proceeds from this offering, we intend to invest the net proceeds in short-term, interest-bearing, investment-grade securities, certificates of deposit or government securities.

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Dividend Policy

We have never declared or paid cash dividends on our common stock. We currently intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination to pay dividends will be made at the discretion of our board of directors after taking into account various factors, including our financial condition, operating results, current and anticipated cash needs, the requirements of any then-existing debt instruments and other factors the board of directors deems relevant.

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Capitalization

The following table sets forth our cash and cash equivalents and capitalization as of December 31, 2013:

- on an actual basis;
- on a pro forma basis to give effect to the automatic conversion of all outstanding shares of our preferred stock into an aggregate of 12,002,329 shares of common stock upon the closing of this offering, calculated based upon accrued dividends through December 31, 2013, and the filing of our amended and restated certificate of incorporation upon the closing of this offering; and
- on a pro forma as adjusted basis to give further effect to the sale of 5,882,353 shares of our common stock offered in this offering, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

You should read this information together with our financial statements and related notes appearing elsewhere in this prospectus and the information set forth under the heading Selected Financial Data and Management s Discussion and Analysis of Financial Condition and Results of Operations .

	As of December 31, 2013		
	Actual	Pro Forma	Pro Forma, as Adjusted
Cash and cash equivalents	$ 21,215,228	$ 21,215,228	$ 111,411,521
Series A redeemable convertible preferred stock, par value $0.00001 per share; 734,538 shares authorized, issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted (Aggregate liquidation preference of $39,367,094 at December 31, 2013)	$ 39,367,094	$	$
Series B redeemable convertible preferred stock, par value $0.00001 per share; 1,287,525 shares authorized, issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted (Aggregate liquidation preference of $21,031,365 at December 31, 2013)	21,257,044		
Series C redeemable convertible preferred stock, par value $0.00001 per share; 3,428,572 shares authorized, 3,302,885 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted (Aggregate liquidation preference of $97,202,997 at December 31, 2013)	97,202,997		
Stockholders deficit:			
Preferred Stock, par value $0.00001 per share; no shares authorized, issued and outstanding, actual, 25,000,000 shares authorized, no shares issued and outstanding pro forma and pro forma as adjusted			
Common stock, par value $0.00001 per share; 14,700,000 shares authorized, 1,383,345 shares issued and outstanding, actual; 175,000,000 shares authorized, 13,385,674 shares issued and outstanding, pro forma and 175,000,000 shares authorized, 19,268,027 shares issued and outstanding, pro forma as adjusted	14	134	193
Additional paid-in capital		94,461,590	184,657,824
Accumulated deficit	(127,072,071)	(63,706,646)	(63,706,646)
Total stockholders (deficit) equity	(127,072,057)	30,755,078	120,951,371

Total capitalization	$ (105,856,829)	$ 51,970,306	$ 232,362,892

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The actual, pro forma and pro forma as adjusted information set forth in the table above excludes the following:

- 1,251,398 shares of our common stock issuable upon the exercise of stock options outstanding as of December 31, 2013 at a weighted-average exercise price of $1.01 per share;
- 155,108 shares of common stock reserved for issuance pursuant to future equity awards under our Amended and Restated 2008 Equity Incentive Plan;
- 1,785,000 shares of common stock reserved for future issuance under our 2014 Incentive Plan; and
- 112,853 shares of common stock issuable upon conversion of our Series C preferred stock with respect to dividends accrued between December 31, 2013 and the consummation of the offering.

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Dilution

If you invest in our common stock in this offering, your ownership interest will be diluted to the extent of the difference between the initial public offering price per share of our common stock in this offering and the pro forma as adjusted net tangible book value per share of our common stock after this offering.

We had a historical net tangible book value of $(127.1) million, or $(91.86) per share of common stock, as of December 31, 2013. Our historical net tangible book value represents total tangible assets less total liabilities and redeemable convertible preferred stock. Our historical net tangible book value per share is our historical net tangible book value, divided by the number of shares of our common stock outstanding as of December 31, 2013.

The pro forma net tangible book value of our common stock as of December 31, 2013 was $30.8 million, or $2.30 per share of our common stock. Pro forma net tangible book value represents the amount of our total tangible assets less our total liabilities, divided by the pro forma number of shares of our common stock outstanding after giving effect to an assumed conversion as of December 31, 2013 of our outstanding preferred stock into an aggregate of 12,002,329 shares of common stock.

After giving further effect to the sale of 5,882,353 shares of common stock in this offering, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value would have been approximately $121.0 million, or approximately $6.28 per share of common stock. This represents an immediate increase in pro forma net tangible book value of $3.98 per share to our existing stockholders and an immediate dilution of $10.72 per share to investors participating in this offering. If the underwriters exercise their option to purchase additional shares, you will experience further dilution. Dilution per share to new investors is determined by subtracting pro forma net tangible book value per share after this offering from the initial public offering price per share paid by new investors. The following table illustrates this dilution on a per share basis:

Assumed initial public offering price per share		$ 17.00
Historical net tangible book value per share as of December 31, 2013	$ (91.86)	
Increase attributable to the pro forma adjustments described above	94.16	
Pro forma net tangible book value per share as of December 31, 2013	2.30	
Increase in pro forma net tangible book value per share attributable to new investors	3.98	
Pro forma as adjusted net tangible book value per share after this offering		6.28
Dilution per share to new investors		$ 10.72

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The following table summarizes, on a pro forma as adjusted basis as of December 31, 2013, the number of shares of common stock purchased from us, the total consideration and the average price per share paid by existing stockholders (giving effect to the conversion of all outstanding shares of our preferred stock into 12,002,329 shares of common stock as of December 31, 2013) and by investors participating in this offering, before deducting underwriting discounts and commissions and estimated offering expenses, at the initial public offering price of $17.00 per share. As the table illustrates, new investors purchasing shares in this offering will pay an average price per share substantially higher than our existing stockholders paid.

	Shares purchased		Total consideration		
	Number	Percent	Amount	Percent	Average price per share
Existing stockholders	13,385,674	69.5%	$ 92,659,355	48.1%	$ 6.92
New investors	5,882,353	30.5%	100,000,001	51.9%	$ 17.00
Total	19,268,027	100%	192,659,356	100%	$ 10.00

If the underwriters exercise their option to purchase additional shares in full, pro forma as adjusted net tangible book value as of December 31, 2013 will increase to $134.9 million, or $6.69 per share, representing an increase to existing stockholders of $4.39 per share, and there will be an immediate dilution of an $10.31 per share to new investors.

The number of shares of common stock to be outstanding after this offering is based on the number of shares outstanding as of December 31, 2013 and excludes the following:

- 1,251,398 shares of common stock issuable upon the exercise of outstanding stock options having a weighted-average exercise price of $1.01 per share;
- 155,108 shares of common stock reserved for issuance pursuant to future equity awards under our Amended and Restated 2008 Equity Incentive Plan;
- 1,785,000 shares of common stock reserved for future issuance under our 2014 Incentive Plan; and
- 112,853 shares of common stock issuable upon conversion of our Series C preferred stock with respect to dividends accrued between December 31, 2013 and the consummation of the offering.

New investors will experience further dilution if any of our outstanding options are exercised, new options are issued and exercised under our equity incentive plans or we issue additional shares of common stock, other equity securities or convertible debt securities in the future.

Certain of our existing stockholders and their affiliated entities, including holders of more than 5% of our common stock, have agreed to purchase an aggregate of 887,929 shares of our common stock in this offering at the initial public offering price. For dilution purposes, the shares purchased and consideration paid by those stockholders in this offering at the initial public offering price set forth in the foregoing discussion and tables are reflected as shares purchased and consideration paid by new investors.

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Selected Financial Data

The selected statements of operations data for the years ended December 31, 2012 and 2013, the period from February 27, 2007 (inception) to December 31, 2013 and the balance sheet data as of December 31, 2012 and 2013 are derived from our audited financial statements included elsewhere in this prospectus. You should read this data together with our financial statements and related notes included elsewhere in this prospectus and the information under the captions Selected Financial 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,		Period from February 27, 2007 (inception) to December 31, 2013
	2012	2013	
	(dollars in thousands, except per share data)		
Consolidated statements of operations data:			
Revenue	$	$	$
Expenses:			
Research and development	5,632	10,781	51,748
General and administrative	2,891	5,152	15,269
Total expenses	8,523	15,933	67,017
Loss from operations	(8,523)	(15,933)	(67,017)
Other income, net	327	2,766	3,975
Net loss	$ (8,196)	$ (13,167)	$ (63,042)
Net loss per share applicable to common stockholders basic and diluted[1]	$ (27.82)	$ (126.94)	$ (481.04)
Weighted-average number of common shares used in net loss per share applicable to common stockholders basic and diluted		544,002	
Pro forma net loss per share applicable to common stockholders basic and diluted (unaudited)[1]		$ (1.31)	
Pro forma weighted-average number of common shares used in pro forma net loss per share applicable to common stockholders basic and diluted (unaudited)		10,132,528	

(1) See Note 2 within the notes to our financial statements appearing elsewhere in this prospectus for a description of the method used to calculate basic and diluted net loss per share of common stock. Pro forma basic and diluted net loss per share of common stock is calculated by dividing net loss attributable to common stockholders, excluding the impact of gains (losses) on the extinguishment of preferred stock, accretion of preferred stock and including the impact of compensation expense associated with awards of restricted stock that contain a performance condition wherein vesting is contingent upon our consummation of a Liquidity Event by the pro forma weighted-average number of common shares outstanding.

	December 31,	
	2012	2013
	(in thousands)	
Balance Sheet Data:		
Cash and cash equivalents	$ 1,641	$ 21,215

Working capital (deficit)	(2,679)	29,529
Total assets	2,244	34,665
Redeemable convertible preferred stock	56,909	157,827
Deficit accumulated during the development stage	(59,588)	(127,072)
Total stockholders deficit	(59,588)	(127,072)

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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 prospectus. Some of the information contained in this discussion and analysis or set forth elsewhere in this prospectus, including information with respect to our plans and strategy for our business, 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 prospectus, 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 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. Our lead product candidate, AKB-6548, is being developed as a once-daily oral therapy that has successfully completed a Phase 2a proof of concept study demonstrating that AKB-6548 safely and predictably raised hemoglobin levels in patients with anemia secondary to chronic kidney disease, or CKD, not requiring dialysis.

We are conducting a Phase 2b trial for AKB-6548 in patients with anemia secondary to CKD who are not dependent on dialysis and expect data to be available in the fourth quarter of 2014. We have also initiated a development program for patients dependent on dialysis. If the results of our Phase 2b trial are positive, we would expect to initiate Phase 3 trials for anemia secondary to CKD in 2015, and would anticipate submitting an NDA for AKB-6548 in the United States by 2018 if the Phase 3 data are favorable.

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.

Since our inception in 2007, we have devoted substantially all 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 the private placement of preferred stock, common stock and convertible notes.

In December 2011, we spun out 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 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 $8.2 million and $13.2 million for the years ended December 31, 2012 and 2013, respectively. Substantially all 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 expenses and increasing 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 2b trial and prepare for a future Phase 3 development program of AKB-6548 for the treatment of anemia secondary to CKD;

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seek regulatory approvals for our product candidates that successfully complete clinical trials;

have our product candidates manufactured for clinical trials and for commercial sale;

establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval;

initiate additional preclinical, clinical or other studies 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 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 such 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.

Financial Operations Overview

Revenue

To date, we have not generated any revenues 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 revenues 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;

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- expenses incurred under agreements with the CROs and investigative sites that will 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 revenues 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, results and cost of completing our Phase 2b clinical trial of AKB-6548;
- assuming AKB-6548 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 trials 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 approval 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 will be required for the completion of clinical development of a product candidate, 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, 2013, we have incurred $51.7 million in research and development expenses. We plan to increase our research and development expenses for the foreseeable future as we continue the development of our AKB-6548 product candidate. Our current and planned research and development activities include the following:

We plan to complete a Phase 2b clinical study during 2014 to examine the safety and efficacy of AKB-6548 in patients with anemia secondary to CKD.

We plan to initiate a Phase 3 development program for AKB-6548 in 2015 for anemia secondary to CKD.

We have begun an efficacy study for AKB-6548 in dialysis patients with anemia, the second indication we will pursue.

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We intend to conduct a Phase 2 clinical trial of AKB-6548 in IAA.

We intend to file an Investigational New Drug, or IND, and begin Phase 1 trials for AKB-6899 and explore its use in oncology and ophthalmology.

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 one program 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 cannot state 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 for our employees in executive, operational, finance and human resource functions. Other general and administrative expenses include facility-related costs and professional fees for directors, accounting and legal services, 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 audit, legal, regulatory and tax-related services associated with maintaining compliance with exchange listing and Securities and Exchange Commission requirements, director and officer insurance premiums, and investor relations costs associated with being a public company. Additionally, if and when we believe a regulatory approval of the first product candidate appears likely, we anticipate an increase in payroll and related expenses as a result of our preparation for commercial operations, especially as it relates to the sales and marketing of our product candidates.

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 prospectus, we believe the following accounting policies to be most critical to the judgments and estimates used in the preparation of our financial statements.

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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 supplies.

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 the agreements can 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 this offering, stock option, common stock and restricted stock values will be 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

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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 development stage company in a very early stage of product development with no revenues 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 performed a sensitivity analysis to determine the impact a 30% increase or decrease in the volatility rate would have on the fair value of each stock-based award, and determined that such a rate change would be immaterial to the calculation of stock-based compensation. We use the simplified method as prescribed by the SEC Staff Accounting Bulletin No. 107, *Share-Based Payment,* to calculate the expected term for options granted to employees as we do not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. The expected term is applied to the stock option grant group as a whole, as we do not expect substantially different exercise or post-vesting termination behavior among our employee population. For options granted to non-employees, we utilize the contractual term of the arrangement as the basis for the expected term assumption. The risk-free interest rate is based on a treasury instrument whose term is consistent with the expected life of the stock options. The expected dividend yield is assumed to be zero as we have never paid dividends and have no current plans to pay any dividends on our common stock, similar to our peer group.We estimate grant date fair value of restricted stock awards with corresponding promissory notes using the Black-Scholes option pricing model. The grant date fair value of restricted stock award grants without a promissory note and awards of common stock is 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 are 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. These awards are referred to as promissory note options in the tables below.

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We have computed the fair value of employee and non-employee stock options at date of grant using the following weighted-average assumptions:

	Year Ended December 31,	
	2012	2013
Expected volatility	73.00%	79.00%
Expected term (in years) employee options	6.25	6.25
Expected term (in years) non employee options	10	10
Expected term (in years) promissory note options	5	5
Risk-free interest rate	0.95%	1.71%
Expected dividend yield	0.00%	0.00%
Expected dividend yield promissory note options	6.00%	3.00%

The following table presents the grant dates, number of underlying shares and related exercise prices or purchase prices of stock options granted and restricted stock awards issued between January 1, 2011 and December 31, 2013, along with the fair value per share utilized to calculate stock-based compensation expense:

Year of grant	Type of award	Number of shares	Exercise price (options) or purchase price (promissory note options) per share	Retrospective common stock fair value per share as of grant date
2011	Option	42,577	0.86	1.09
2011	Restricted Stock Award	254,457[(1)]	N/A	1.09
2011	Common Stock Awards	39,000	N/A	1.09
2012	Option	70,789	0.86	1.09
2012	Restricted Stock Award	52,582	N/A	1.00
2013	Option	921,107	0.47-3.77	3.77-7.42
2013	Restricted Stock Award	53,835	N/A	0.89
2013	Common Stock Awards	176,716	N/A	3.77-7.42

(1) Represents promissory note options, as described above.

Stock-based compensation totaled approximately $0.1 million for the year ended December 31, 2012 and approximately $1.6 million for the year ended December 31, 2013. As of December 31, 2013, we had approximately $3.4 million of total unrecognized compensation expense related to stock options and approximately $0.1 million of total unrecognized compensation expense related to restricted stock grants with only service based vesting conditions, which are expected to be recognized over a weighted-average remaining vesting period of approximately 2.3 years and 1.8 years, respectively. As of December 31, 2013, we also had approximately $3.9 million of total unrecognized compensation expense related to restricted stock grants with performance conditions which will be recognized commencing upon the occurrence of a Liquidity Event.

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.

Fair Value of Stock Options

We have historically granted stock options at exercise prices not less than the fair value of our common stock as of the actual date of grant. As there has been no public market for our common stock to date, the estimated fair value of our common stock has been determined contemporaneously by our board of directors based on valuation estimates provided by third party valuations prepared for purposes of income tax reporting under Section 409A of the Internal Revenue Code.

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In October 2013, in consideration of the improving market for initial public offerings by biopharmaceutical companies, our board of directors directed us to begin preparation of a registration statement for an initial public offering. We selected underwriters and held an organizational meeting on November 18, 2013. We believe these events increased the probability of an early initial public offering.

As a result, in connection with the preparation of our financial statements for the years ended December 31, 2012 and 2013, and the period from February 27, 2007 (date of inception) to December 31, 2013, we reexamined the valuation of our common stock. In connection with that reexamination, we prepared retrospective appraisals of the fair value of our common stock for financial reporting purposes as of December 31, 2012 March 31, 2013 and September 30, 2013. Prior to 2013, our contemporaneous valuations were prepared to comply with Section 409A of the Internal Revenue Code. As a result, the contemporaneous valuations were not performed under the fair value framework as set forth under ASC 820 and did not take into account the guidance provided in the American Institute of Certified Public Accountants (AICPA) Technical Practice Aid, Valuation of Privately-Held-Company Equity Securities Issued as Compensation. Accordingly, the contemporaneous valuations had limited value for purposes of financial reporting under U.S. GAAP. Therefore, in connection with the preparation of our financial statements, we re-assessed the fair value of our common stock for financial reporting purposes by having retrospective valuations performed in accordance with the fair value framework under ASC 820 and the AICPA Technical Practice Aid. We believe that the valuation methodologies used in the retrospective valuations are reasonable and consistent with the AICPA Practice Aid. The fair values of our common stock shown in the table above reflect these retrospective valuations.

The table below summarizes the common stock values determined in our contemporaneous and retrospective valuations:

Date	Contemporaneous	Retrospective
December 31, 2012	$ 0.86	$ 0.57
March 31, 2013	n/a	$ 0.89

December 31, 2012 Retrospective Valuation

For the retrospective valuation at December 31, 2012, we used the guideline public company method under the market approach to value our equity. We estimated our equity value based on a multiple of paid-in capital as indicated by a group of guideline public companies. In our selection of guideline public companies, we took into account each candidate s stage of clinical development and the targeted indications for drugs in development. We used the option-pricing method, or OPM, to allocate the value of our equity among our preferred and common stock. We applied a discount for lack of marketability to the value indicated for our common stock. Our estimate of the appropriate discount for lack of marketability took into consideration put option methodologies consistent with the AICPA Practice Aid.

The OPM treats common stock and preferred stock as call options on the total equity value of a company, with exercise prices based on the value thresholds at which the allocation among the various holders of a company s securities changes. Under this method, the common stock has value only if the funds available for distribution to stockholders exceed the value of the liquidation preference at the time of a liquidity event, such as a strategic sale, merger or IPO. The common stock is modeled as a call option on the underlying equity value at a predetermined exercise price. In the model, the exercise price is based on a comparison with the total equity value rather than, as in the case of a regular call option, a comparison with a per share stock price. Thus, common stock is considered to be a call option with a claim on the enterprise at an exercise price equal to the remaining value immediately after the preferred stock is liquidated. The OPM uses the Black-Scholes option pricing model to price the call options. This model defines the securities fair values as functions of the fair value of a company s equity as of an appraisal date and uses assumptions such as the anticipated timing of a potential liquidity event and the estimated volatility of the equity securities.

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The following table summarizes the significant assumptions used in the OPM to determine the fair value of our common stock as of December 31, 2012:

December 31, 2012 retrospective valuation	
Key assumptions	
Years to liquidity	1.96
Annual volatility	58%
Risk-free interest rate	0.25%
Discount for lack of marketability (DLOM)	19%

Based on these assumptions, we estimated the fair value of our common stock to be $0.57 as of December 31, 2012.

March 31, 2013 Retrospective Valuation

For the retrospective valuation at March 31, 2013, we used the hybrid method to value our common stock. The hybrid method is a hybrid between the probability-weighted expected returns method and the OPM. We considered an IPO scenario, in which our preferred shares convert to common stock, and a second scenario, in which equity value is allocated using the OPM. We used the guideline public company method under the market approach to value our equity. We estimated our equity value based on a multiple of paid-in capital as indicated by a group of guideline public companies. In addition, we estimated the value of our equity securities in association with an IPO. We considered the enterprise values of guideline public companies and the pricing of IPOs completed by clinical stage drug development companies in the year preceding our appraisal date. For each of the IPO companies, we considered the increase, or step-up, in per share value from the preferred financing preceding the IPO to the common stock value in the IPO. We also considered the equity value of each IPO company, not including the proceeds of the IPO.

The following table summarizes the significant assumptions used in the hybrid method to determine the fair value of our common stock as of March 31, 2013:

March 31, 2013 retrospective valuation	IPO	OPM
Key assumptions		
Probability weighting	5%	95%
Years to liquidity	1.71	1.71
Weighted-average cost of capital	20%	
Annual volatility		59%
Risk-free interest rate		0.22%
Discount for lack of marketability (DLOM)	18%	18%
Estimated per share present value of non-marketable common stock (before probability weighting)	$ 5.57	$ 1.00

Based on these assumptions, we estimated the fair value of our common stock to be $0.89 as of March 31, 2013.

The estimated per share fair value of our common stock calculated in our March 31, 2013 retrospective valuation of $0.89 per share increased from the December 31, 2012 valuation of $0.57 per share primarily due to the following factors:

Litigation to protect our intellectual property rights in Europe was decided in our favor.

We made progress toward completing a Series C preferred stock financing, enhancing our prospects for securing the capital needed for clinical trials prior to an IPO.

We raised additional capital by issuing Series X preferred shares, and the terms of the Series X shares were revised to the benefit of the common stockholders.

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September 30, 2013 Valuation

For the contemporaneous valuation at September 30, 2013, we used the probability-weighted expected returns method (PWERM). Under PWERM, the values of the various equity securities are estimated based upon an analysis of future values for the enterprise, assuming various future outcomes. Share value is based upon the probability-weighted present value of expected future investment returns, considering each of the possible future outcomes available to the enterprise, as well as the rights of each share class.

We considered three scenarios: an IPO, a sale of the Company and a liquidation of the Company s assets. For the IPO scenario, we considered the enterprise values of guideline public companies and the pricing of IPOs completed by clinical stage drug development companies in the year preceding our appraisal date. For each of the IPO companies, we considered the increase, or step-up, in per share value from the preferred financing preceding the IPO to the common stock value in the IPO. We also considered the equity value of each IPO company, not including the proceeds of the IPO. For the sale scenario, we assumed a market participant acquisition premium (MPAP) to the IPO value. Our estimate of the MPAP took into account the premiums observed in eight acquisitions completed in 2013 of publicly-traded clinical stage drug development companies. For the liquidation scenario, we considered a value equal to the amount invested in our Series C preferred stock.

The following table summarizes the significant assumptions used in the PWERM to determine the fair value of our common stock as of September 30, 2013:

	IPO	Sale	Liquidation
Probability	33%	25%	42%
Years to Liquidity	0.48	1.25	1.75
Weighted-average cost of capital	20%	20%	20%
Discount for lack of marketability (DLOM)	12%	20%	NA

Based on these assumptions, we estimated the fair value of our common stock to be $3.77 as of September 30, 2013.

The estimated per share fair value of our common stock calculated in our September 30, 2013 valuation of $3.77 per share increased from the March 31, 2013 valuation of $0.89 per share primarily due to the following factors:

- We completed our Series C preferred stock financing.
- We completed our Phase 2a dose-ranging study of AKB-6548 in patients with stage 3 and 4 CKD.
- Capital market conditions for biotechnology companies improved, as evidenced by an increase in the number of IPOs and their IPO valuations.
- We estimated that the probability of the Company completing an IPO increased.

December 31, 2013 Valuation

For the contemporaneous valuation at December 31, 2013, we used the PWERM method.

We considered three scenarios: an IPO, a sale of the Company and a liquidation of the Company s assets. For the IPO scenario, we considered the enterprise values of guideline public companies and the pricing of IPOs completed by clinical-stage drug development companies in the year preceding our appraisal date. For each of the IPO companies, we considered the increase, or step-up, in per share value from the preferred financing preceding the IPO to the common stock value in the IPO. We also considered the equity value of each IPO company, not including the proceeds of the IPO. For the sale scenario, we assumed a MPAP to the IPO value. Our estimate of the MPAP took into account the premiums observed in nine acquisitions completed in 2013 of publicly-traded clinical-stage drug development companies. For the liquidation scenario, we considered a value equal to the amount invested in our series C preferred stock.

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The following table summarizes the significant assumptions used in the PWERM to determine the fair value of our common stock as of December 31, 2013:

	IPO	Sale	Liquidation
Probability	70%	15%	15%
Years to Liquidity	0.22	1.00	1.50
Weighted-average cost of capital	20%	20%	20%
DLOM	8%	18%	NA

Based on these assumptions, we estimated the fair value of our common stock to be $7.42 as of December 31, 2013.

The estimated per share fair value of our common stock calculated in our December 31, 2013 valuation of $7.42 per share increased from the September 30, 2013 valuation of $3.77 per share primarily due to the increase in the probability of completing an IPO.

There are significant judgments and estimates inherent in the determination of these valuations. These judgments and estimates include assumptions regarding our future performance, including the successful enrollment and completion of our clinical studies as well as the determination of the appropriate valuation methods. If we had made different assumptions, our stock-based compensation expense could have been different. The foregoing valuation methodologies are not the only methodologies available and they will not be used to value our common stock once this offering is complete. We cannot make assurances as to any particular valuation for our common stock. Accordingly, we caution you not to place undue reliance on the foregoing valuation methodologies as an indicator of future stock prices.

The Company has recognized the following compensation cost related to employee and non-employee based stock option, restricted stock and common stock activity:

Year Ended	Research and Development	General and Administrative	Total
2013	$ 110,686	$ 1,453,073	$ 1,563,759
2012	52,768	69,573	122,341
2011	175,418	132,011	307,429

Initial Public Offering Price

The initial public offering price of $17.00 per share was determined as a result of negotiations between us and the underwriters. In comparison, our estimate of the fair value of our common stock was $7.42 per share as of December 31, 2013. We note that, as is typical in initial public offerings, the initial public offering price was not derived using a formal determination of fair value, but was determined by negotiation between us and the underwriters. The difference between the fair value of our common stock as of December 31, 2013, which is the most recent common stock valuation date, and the initial public offering price is primarily due to the following factors:

the increased enrollment of our Phase 2b trial (which is currently over 80% enrollment as compared to 56% enrollment as of the most recent common stock valuation date);

updated results obtained in January from our pharmacokinetics study in subjects on dialysis, which has led us to establish a plan to administer once-daily doses of AKB-6548 in our open label Phase 2 study in subjects on dialysis instead of dosing three times weekly;

the initiation in January of a thorough QT, or TQT, study to ensure that AKB-6548 does not affect the cardiac conduction cycle and completion of the first cohort of patients in this study. Successful completion of the TQT study will allow for a Phase 3 program with reduced cardiac monitoring;

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in the public markets we believe there are investors who may apply more qualitative and subjective valuation criteria to certain of our clinical assets than the valuation methods applied in our valuations, although there can be no assurance that this will in fact be the case. As described in the prospectus, as a private company we used a more quantitative methodology to determine the fair value of our common stock, and this methodology differs from the methodology used to determine the estimated price range for this offering. The estimated price range for this offering was not derived using a formal determination of fair value, but rather was determined following negotiations between us and the underwriters;

the estimate of the fair value of our common stock as of December 31, 2013 utilizes a probability-weighted, discounted approach. As such, the resulting fair value per share reflects the potential for alternative liquidity events, including sale and dissolution scenarios, which inherently decreases the estimated fair value per share due to the combination of the mix of other expected equity values discounted for their future value. Our estimate of the fair value of our common stock as of December 31, 2013 was discounted using a weighted average cost of capital of 20% and an estimate of probability for an IPO of 70%, whereas our estimated price range was not reduced by the expected future business values (discounted to present value) from other potential future liquidity events and assumes the completion of the offering;

the initial public offering price necessarily assumes that the initial public offering has occurred and a public market for our common stock has been created, and therefore excludes any discount for lack of marketability of our common stock, which was factored in our valuations. Our December 31, 2013 valuation included an illiquidity discount of 8% to 18%;

in-depth and confirmatory discussions with our underwriters regarding the estimated price range did not take place until February 21, 2014, which was after they received positive feedback from potential investors regarding our testing-the-waters meetings held after December 31, 2013;

improved capital market conditions for companies in our industry, as evidenced by a recent increase in the number of public offerings by such companies and in the initial public offering valuations of such companies compared to the valuations in their most recent pre-IPO equity financing. Since our most recent common stock valuation date, the NASDAQ Biotechnology Index has increased by more than 18%;

the price that investors are willing to pay in this offering may take into account other things that have not been expressly considered in our prior valuations, are not objectively determinable and that valuation models are not able to quantify;

the conversion of all outstanding shares of our preferred stock into common stock upon completion of this offering, thus eliminating the superior rights and preferences of our preferred stock as compared to our common stock; and

the addition of Michael S. Wyzga, a seasoned biotechnology executive, to our board of directors and chairman of the audit committee, who will be available as a resource to support our senior management team.

Emerging Growth Company Status

The JOBS Act, permits an emerging growth company such as us to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies. We are choosing 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.

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Recently Adopted Accounting Pronouncements

In February 2013, the FASB issued guidance to provide information about the amounts reclassified out of accumulated other comprehensive income, or AOCI, by component. An entity is required to present, either on the face of the financial statements or in the notes, significant amounts reclassified out of AOCI by the respective line items of net income, but only if the amount reclassified is required to be reclassified in its entirety in the same reporting period. For amounts that are not required to be reclassified in their entirety to net income, an entity is required to cross-reference to other disclosures that provide additional details about those amounts. On January 1, 2013, we adopted this standard, which had no impact on our financial position or results of operations.

Results of Operations

Comparison of the Years Ended December 31, 2012 and 2013

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

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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, 2013, we had an accumulated deficit of $127.1 million. We anticipate that we will continue to incur losses for at least the next several years. We expect that our research and development and general and administrative expenses will continue to increase and, as a result, we will need additional capital to fund our operations, which we may raise through a combination of equity offerings, debt financings, other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements.

We have funded our operations principally from the sale of common stock, preferred stock and convertible notes. As of December 31, 2013, we had cash and cash equivalents of approximately $21.2 million. Cash in excess of immediate requirements is invested in accordance with our investment policy, primarily with a view to liquidity and capital preservation. Investments, 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,	
	2012	2013
	(in thousands)	
Net cash provided by (used in):		
Operating activities	$ (7,211)	$ (11,332)
Investing activities	1,366	(11,425)
Financing activities	2,475	42,331
Net (decrease) increase in cash and cash equivalents	$ (3,370)	$ 19,574

Operating Activities. The net cash used in operating activities was $11.3 million for the year ended December 31, 2013, and consisted primarily of a net loss of $13.2 million adjusted for non-cash items including gain on extinguishment of debt of $2.4 million, stock-based compensation expense of $1.6 million, amortization of debt discount of $0.8 million and a net increase in operating assets and liabilities of $1.9 million. The significant items in the change in operating assets and liabilities include increases in accounts payable and accrued expenses of $2.3 million, offset by a decrease in prepaid expenses, other current assets and other assets of $0.3 million. The increase in accounts payable and accrued expenses is driven by professional fees incurred in connection with our planned initial public offering.

The net cash used in operating activities was $7.2 million for the year ended December 31, 2012, and consisted primarily of a net loss of $8.2 million adjusted for non-cash items including amortization of debt issue costs and debt discount of $1.7 million and stock-based compensation expense of $0.1 million and a net decrease in operating assets and liabilities of $0.8 million. The significant items in the change in operating assets and liabilities include a decrease in accounts payable and accrued expenses of $1.0 million, offset by an increase in prepaid expenses and current assets of $0.2 million.

Investing Activities. Net cash provided by (used in) investing activities consisted of purchases of fixed assets, purchases of marketable securities, and proceeds from the maturity and sale of marketable securities. Net cash used in investing activities for the year ended December 31, 2013 was $11.4 million and was comprised primarily of purchases of investments of $13.4 million, offset by proceeds from maturities of investments of $2.0 million. Net cash provided by investing activities for the year ended December 31, 2012 was $1.4 million and consisted completely of proceeds from sales of investments.

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Financing Activities. Net cash provided by financing activities for the year ended December 31, 2013 was $42.3 million and consisted primarily of $41.2 million of proceeds from the issuance of preferred stock, $2.5 million of proceeds from the issuance of 25,000 shares of Series X preferred stock, partially offset by stock issuance costs of $1.2 million and initial public offering related costs of $0.2 million. Net cash provided by financing activities for the year ended December 31, 2012 is the result of the sale of 25,000 shares of our Series X preferred stock for net proceeds of $2.5 million.

Operating Capital Requirements

To date, we have not generated any revenue from product sales. We do not know when, or if, we will generate any revenue from product sales. We 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 of the risks incident in 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. Upon the closing of this offering, we expect to incur additional costs associated with operating as a public company. We anticipate that we will need substantial additional funding in connection with our continuing operations.

We believe that the net proceeds from this offering and our existing cash and cash equivalents 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, increased fixed payment obligations and these securities may have rights senior to those of our common stock. If we incur indebtedness, we could become subject to covenants that 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 prove to be wrong, and we could utilize our available capital resources sooner than we currently expect. Our future funding requirements, both near and long-term, will depend on many factors, including, but not limited to:

- the rate of progress, results and cost of completing our Phase 2b clinical trial of AKB-6548 and our operating costs incurred as we conduct these trials and through our end of Phase 2 meeting with the FDA, and equivalent meetings with the EMA and other regulatory authorities;

- assuming positive results from our current Phase 2b trial, the scope, size, rate of progress, results and costs of initiating and completing our Phase 3 development program of AKB-6548;

assuming favorable clinical results, the cost, timing and outcome of our efforts to obtain marketing approval for AKB-6548 in the United States 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;

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- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for AKB-6899 and any 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 trials are successful and the outcome of regulatory review of AKB-6899;
- 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 in preparation for regulatory approval 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, prosecuting patent applications, maintaining, defending and enforcing our intellectual property rights, including litigation costs and the outcome of such litigation;
- the timing, receipt, and amount of sales of, or royalties on, our future products, if any;
- the need to implement additional infrastructure and internal systems; and
- the extent to which we acquire or in-license other products or technologies.

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, we 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 commences and rental payments begin in January 2014. We will record a deferred lease obligation in 2014 which will represent the cumulative difference between actual facility lease payments and lease expense recognized ratably over the lease period. We did not have rent expense associated with this lease in 2013.

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

At December 31, 2013, our 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	$ 12,600	$ 3,850	$ 8,750	$	$
Operating Lease Obligations	1,117,280	344,699	772,581		
Total	$ 1,129,880	$ 348,549	$ 781,331	$	$

We contract with various organizations to conduct research and development activities with remaining contract costs to us of $4.5 million at December 31, 2013. The scope of services under the research and development contracts can be modified and the contracts cancelled by either party upon written notice.

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Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined in the rules and regulations of the Securities and Exchange Commission.

Quantitative and Qualitative Disclosures About Market Risks

We are exposed to market risk related to changes in interest rates. As of December 31, 2012 and 2013, we had cash and cash equivalents and investments of $1.6 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.

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Business

Overview

We are a biopharmaceutical company focused on the development of novel proprietary therapeutics based on HIF biology and the commercialization of these products for patients with kidney disease. HIF is the primary regulator of the production of RBCs in the body and a potentially 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 2a proof of concept study demonstrating that AKB-6548 safely and predictably raised hemoglobin levels in patients with anemia secondary to CKD not requiring dialysis.

We are conducting a Phase 2b trial for AKB-6548 in patients with anemia secondary to CKD who are not dependent on dialysis and expect data to be available in the fourth quarter of 2014. We have also initiated a development program for patients dependent on dialysis. If the results of our Phase 2b trial are positive, we would expect to initiate Phase 3 trials for anemia secondary to CKD in 2015, and would anticipate submitting an NDA for AKB-6548 in the United States by 2018 if the Phase 3 data are favorable.

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 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-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 eight clinical trials across four separate patient populations: healthy volunteers and patients with CKD stages 3, 4 and 5 (non-dialysis). Our largest study was a Phase 2a trial in 91

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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.

Our ongoing Phase 2b trial explores a dosing approach for AKB-6548 to enable subjects with anemia secondary to CKD to appropriately and safely raise hemoglobin levels. As of February 28, 2014, we had enrolled over 80% of our targeted 200 patients in this study at investigational sites in the United States, with data expected in the fourth quarter of 2014. With positive data, we plan to progress to Phase 3 global registration studies for AKB-6548 in patients with anemia secondary to CKD. We anticipate the design of the Phase 3 studies will mirror the Phase 2b study, except that they will be longer and larger in size, positioning us to file for approval in the United States by 2018.

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 of 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, including IAA and anemia of congestive heart failure.

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 Corp. s renal division which grew to over $1 billion in annual revenue under his leadership, and is current 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 executive team also includes Robert Shalwitz, M.D., CMO and co-founder of Akebia. Dr. Shalwitz is an academic pediatric endocrinologist and has extensive industry experience developing novel pharmaceuticals at Abbott Laboratories and Reliant Pharmaceuticals. He has developed extensive knowledge of HIF biology over his career, particularly over the past seven years in leading development at Akebia.

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 plan to complete the Phase 2b trial that is currently enrolling in the United States. We intend to initiate a Phase 3 development program in 2015 following our end of Phase 2 meeting with the 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 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 would anticipate submitting an NDA for AKB-6548 in the United States by 2018 if the Phase 3 data are favorable.

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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.

Continue to develop AKB-6548 for further indications. We plan to initiate, in the first half of 2014, a Phase 2 study for AKB-6548 in dialysis patients with anemia, the second indication we intend to pursue. Additionally, we plan to evaluate the product candidate in IAA and other indications.

Advance our earlier stage pipeline asset. 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 IND application and begin Phase 1 trials to determine its potential use in oncology and ophthalmology.

Acquire or in-license additional nephrology products. If we are able to successfully launch AKB-6548, we will look to leverage our commercial infrastructure with additional products that would be prescribed by nephrologists.

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

Our Product Candidates

The following chart depicts our HIF-based product candidates, their indications and their current development. We have not conducted separate Phase 1 trials for anemia secondary to CKD in patients on dialysis or for patients with IAA. However, we expect to rely upon data from completed Phase 1 trials of AKB-6548 for anemia secondary to CKD in patients not on dialysis to initiate Phase 2 clinical trials of AKB-6548 for these indications.

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.

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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 subject 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. As shown in the table below, the prevalence of anemia is associated with the severity of CKD in this population.

There are many causes of CKD, the most common of which are diabetes 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

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(maternal diabetes mellitus, low birth weight and small-for-gestational-age status). Beyond the United States, 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 both oxygen and carbon dioxide.

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 with iron supplements. Based on the reported revenues of companies that market and sell rESAs, we estimate that global

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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, which is consistent with the general trend of increasing IV iron. Among U.S. patients receiving IV iron, the mean monthly dose has also increased by 21%. Despite the increased use of IV iron and rate of transfusions, patients are still subject to safety risks related to these alternative treatments to injectable rESAs. The risks of 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 transfusion. The risks of IV iron include hypersensitivity reactions, such as fatal anaphylactic-type reactions.

Currently, there is no scientific consensus regarding 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 randomized controlled trials data 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 with or without minimal doses of injectable rESAs or supplemental iron had better clinical outcomes than subjects assigned to higher hemoglobin targets who failed to reach the assigned level with increasing doses of injectable rESAs and iron. In addition, CKD patients who are 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, but is related to the dose, dose frequency, and dose duration of injectable rESAs.

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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.

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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 boxed 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

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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 reportedly failed to show 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. We expect AKB-6548 to 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

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and improved stabilization of the bone marrow s iron supply, which ensures the proper incorporation of iron into hemoglobin necessary for such 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.

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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 in the treatment of anemia secondary to CKD.

AKB-6548 significantly increases hemoglobin in anemic CKD patients. We have successfully completed a Phase 2a trial, in which AKB-6548 significantly increased hemoglobin levels compared to baseline in a dose-dependent manner across all treatment arms ($p < 0.0001$). 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, meaning that these improvements occur without causing patients hemoglobin to rise 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, such as IAA. AKB-6548 offers the potential of flexible oral dosing that provides a more gradual and reliable means of titration than that of injectable rESAs.

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Ability to stabilize the iron supply to the bone marrow while improving hemoglobin production. In clinical trials, AKB-6548 has demonstrated a dose-related increase in total iron binding capacity, or TIBC.

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 2a study, no drug-related serious adverse events were reported. Dosing was well-tolerated and there was no evidence of undesirable vascular response.

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 eight clinical trials across four separate patient populations: healthy volunteers and patients with CKD stages 3, 4, and 5 (non-dialysis). These clinical trials consisted of four Phase 2a clinical trials and four 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.

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

Study	Subject	Study Design	Dose, Duration[1]	Subjects Treated		Key Findings
		Design		AKB-6548	Placebo	
Phase 1						
CI-0001	Healthy males	Double-blind, placebo-controlled, fasted	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 AE (seven in the AKB-6548 group and three in the placebo group). No SAEs were reported.
CI-0002	Healthy males	Double-blind, placebo-controlled, fasted	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 TEAE. These were evenly distributed across dosing groups. No SAEs were reported.
CI-0006	Healthy males	Randomized, cross-over bioavailability study, fasted	315 mg; single dose of capsule and tablet, with three days 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.
Phase 2						
CI-0003	CKD, Stages 3 & 4	Open-label, fed	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.
CI-0004	CKD, Stages 3 & 4	Open-label	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 TEAEs considered related to study drug. No SAEs were reported.
CI-0005	CKD, Stages 3, 4 & 5, not on dialysis	Double-blind, placebo-controlled	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-0008	Healthy volunteers	Mass Balance	650 mg; single dose	6	0	Though the final study report is not yet complete, the preliminary data supported earlier findings from human and animal studies. The drug was generally well tolerated during this study.
CI-0009	End-stage renal disease (ESRD)	Pharmacokinetics	450 mg dose four hours prior to start of a dialysis session; 450 mg dose two hours after completion of a different dialysis session	12	0	During the study, dosing of the drug was well tolerated, and there was only one SAE, which was considered unrelated to AKB-6548.

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

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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 Association 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 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 in both the modified intent to treat, or MITT, population and the per protocol, or PP, population. 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 ($p<0.0001$) in both the MITT and PP populations. 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.

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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.

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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.

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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.

The principal investigator at the enrolling site for the subject experiencing the SAE is responsible for determining whether a SAE is related to AKB-6548 or not. If the principal investigator is able to determine an alternative reason for the cause of the SAE, then the SAE is generally considered to be unrelated. Upon continuing review of all SAEs from the various clinical studies, a pattern of SAEs may emerge to indicate relatedness. To date, no such pattern has emerged in our AKB-6548 trials.

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).

Ongoing and Planned Clinical Trials

Phase 2b Study (CI-0007)

We are currently enrolling 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 will evaluate the efficacy and safety of AKB-6548 in 200 subjects across 62 U.S. sites. The study will enroll patients who have never received rESA therapy, patients previously treated with rESAs, and patients actively treated with rESAs. Patients will initiate treatment with either 450mg of AKB-6548 or placebo once-daily for 20 weeks. The dose of AKB-6548 will be adjusted in accordance with the patient s hemoglobin response. The primary purpose of this study is to demonstrate an adaptive approach to dosing AKB-6548 that will enable subjects to appropriately raise their hemoglobin from baseline without excessive excursions to greater than 13.0 g/dL. Subjects will be extensively evaluated for clinical and laboratory safety, changes in specific biomarkers, and changes in quality-of-life and neuro-cognitive outcomes. We expect that the results for CI-0007 will enable the final design for Phase 3 studies of AKB-6548. It is anticipated that CI-0007 will be fully enrolled by the second quarter of 2014, and we expect that top line results will be announced in the fourth quarter of 2014.

Patients will be 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 will be adjusted in accordance with the protocol defined Dose Adjustment Guidelines and Algorithm. We will determine optimal dosage, which includes tablet size and number of tablets per dose, and dose adjustment for the Phase 3 studies based on the results from the Phase 2b study. We do not currently anticipate that the range of doses will be significantly changed, but we plan to optimize the algorithm to help maintain hemoglobin in an acceptable range (likely 10.5 to 12 g/dL, subject to review and acceptance by FDA and other regulatory authorities). We plan to further adjust the algorithm to help minimize hemoglobin fluctuation and reduce the frequency of excessive excursions in hemoglobin.

The primary endpoint of our study is the percent of subjects who either (i) achieve or maintain 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 receive injectable rESA or transfusion rescue will be counted as failures and subjects receiving transfusion for a non-rescue reason will be removed from the primary

analysis. Patients will also be analyzed for safety, including AEs, vital signs, electrocardiograms, and laboratory assay results.

Additional assessments to be 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 neurocognitive functioning and patient reported outcomes.

Studies of AKB-6548 in Dialysis Patients

We plan to initiate a multiple dose, open label Phase 2 study in approximately 60 subjects on dialysis in the first half of 2014. The primary endpoint will compare the change in hemoglobin from baseline for two different doses of AKB-6548 given once daily following hemodialysis: 1) 450 mg per dose and 2) 300 mg per dose. The first analysis of change in hemoglobin will be carried out at Week 8, and the second analysis will assess the subsequent 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.

Projected Phase 3 Clinical Trials

Upon completion of our Phase 2b study, and if we receive positive feedback from the FDA, we intend to initiate our Phase 3 studies. We expect that the endpoints, duration, and size of these Phase 3 trials will be based on those used in the Omontys (Peginesatide) approval studies, with modifications to adjust for the shift in focus to CKD in patients not on dialysis, because Omontys was the most recently approved new drug for the treatment of anemia secondary to CKD. Though the primary endpoint for all of the Omontys studies was based on hemoglobin, the total size and duration of the studies were determined by the principal secondary outcome, which was an index of cardiac safety events, or CSEs. The key difference between the clinical program for Omontys and AKB-6548 is that the Omontys trial was primarily designed around patients on dialysis, with only one-third of the subjects being those who were not on dialysis. As a result, the overall rate of CSE events in the Omontys studies is considerably higher than the rate anticipated for AKB-6548 for subjects not on dialysis. Therefore, we believe that approval for AKB-6548 in non-dialysis subjects will require a non-inferiority limit that is higher than the 1.3 required for Omontys for both dialysis and non-dialysis subjects. The endpoints have not yet been agreed upon with FDA or other regulatory bodies.

The primary two studies will be double-blind, randomized, and placebo controlled. The anticipated goal of anemia management in these studies will be to raise hemoglobin levels to greater than 10.5 g/dL and include a rescue component for subjects with declining hemoglobin that uses injectable rESAs in accordance with existing guidelines. In this manner, AKB-6548 will be compared to the existing standard of care for both efficacy and safety. The principle requirement for safety will be to demonstrate non-inferiority for cardiovascular safety of AKB-6548 relative to the standard of care provided to the placebo group. We are designing these clinical studies to be applicable for global development with limited protocol differences between geographic regions. The total number of subjects to be enrolled in the Phase 3 studies will be determined upon agreement with FDA, EMA and other regulatory authorities.

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 Phase 3 studies for the indication of anemia secondary to CKD (not including dialysis) will require approximately three studies and include a total of 2,000 subjects. We estimate that the studies will be two years in duration, with an average subject duration on study drug of 1.25 years.

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Additional Studies

Prior to initiating the Phase 3 studies, we intend to complete a thorough QT, or TQT, study in accordance with FDA guidance to ensure that AKB-6548 does not affect the cardiac conduction cycle. 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. We initiated this study in approximately 50 healthy volunteers in January 2014.

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, two-year carcinogenicity assessments 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 two-year 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.

Additional Indications

The two major additional indications for AKB-6548 are anemia associated with aging (also known as IAA) and anemia secondary to congestive heart failure, or CHF. AKB-6548, with its different mechanism of action, offers a completely new approach to these large markets. Both occur in very large segments of the population and are associated with considerable morbidity and mortality. Anemia affects approximately 10% of individuals age 65 and over, and in those individuals age 85 and older, the percentage is greater than 20%, according to a paper published in 2004 in the peer-reviewed journal *Blood*. Of these, approximately one-third are considered to be IAA. Other causes of anemia in this population include CHF, CKD and nutritional deficiencies. Because injectable rESAs are currently associated with increased cardiovascular events, they have not been successful entering either of these markets.

We anticipate studying both indications by using a fixed, low-dose therapeutic approach which would enable a modest increase in hemoglobin, and minimize the requirement for follow-up assessments. Although we will have extensive dosing information from the CKD studies, additional Phase 2 studies will need to be performed to evaluate the required dose level. In addition, the Phase 2 studies will evaluate cardiac performance and other outcomes that will be critical in Phase 3. It is likely that the study in IAA would be undertaken first, as the mechanism of action of AKB-6548 is well supported by the scientific literature in IAA. Specifically, AKB-6548 is expected to stabilize the limited production of HIF2a in older patients. The primary outcome for this study will focus on quality-of-life outcomes, such as the ability of a subject to perform activities of daily living. In addition, the study will need to evaluate standard measures of morbidity and mortality. An IND has not been filed for AKB-6548 for the treatment of IAA. We expect to file this IND following the conclusion of the Phase 2b clinical trial for AKB-6548 in patients with anemia secondary to CKD who are not dependent on dialysis. We expect to initiate the study following the analysis of the Phase 2b study results, particularly the performance of the drug in patients over the age of 70.

AKB-6899

AKB-6899, another HIFa-stabilizing compound, is a very close relative of AKB-6548. 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

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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 excellent treatment for certain cancers (ovarian, breast, colon, and possibly lung), that could be given in combination with other types of 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. The intended commercial manufacturing route has been successfully scaled up and has produced approximately 40 kg of AKB-6548 drug substance. The drug substance can be readily formulated into compressed tablets using standard USP grade excipients. We have made compressed tablets of varying sizes with no apparent effect on dissolution profile or bioavailability.

The preclinical candidate AKB-6899 has been produced on laboratory scale, but clinical or commercial manufacturing has not been investigated. Based on the similarity of the structure to AKB-6548, similar commercially available starting materials and commercial manufacturing process can be expected.

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 of AKB-6548 and other clinical trials.

A high quality U.S.-based manufacturer will be selected to supply drug product for our Phase 3 development program of AKB-6548 and other clinical trials. Current tableting methods are amenable for scale up to commercial quantities of drug product. To date, 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,

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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 19 allowed applications and issued patents and approximately 39 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. 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 four 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 2027 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 two issued patents and one pending application covering the AKB-6899 composition of matter and pharmaceutical compositions 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 2027 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, three pending applications covering various methods, including, but not limited to, the treatment of cancer or chemotherapy-induced anemia by administration of AKB-6899 in the United States. The expected expiration dates for these method of treatment patent applications are expected to be either 2027 or 2032 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 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

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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, Japan Tobacco, AstraZeneca, 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 as early as 2015 or 2016. 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.

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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.

For example, in January 2012, Hospira, Inc. announced the beginning of its Phase 3 clinical program for its biosimilar rEPO with results anticipated in 2013, and 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 agreement with Amgen 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;

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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 nonclinical 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. 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 submission 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 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 and/or 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.

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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 agency 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 DSMB 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 trials 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 results of nonclinical studies and of the clinical trials, together with other detailed information, including 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.

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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.

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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.

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, clinical trial development may proceed.

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.

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. 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.

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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

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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 h 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, 2013, we had 28 employees, 24 of whom were full-time, eight of whom hold Ph.D. or M.D. degrees, 16 of whom were engaged in research and development activities and 12 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 6,837 square feet of office space in Cambridge, Massachusetts under a lease that expires on December 26, 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.

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Legal Proceedings

We have opposition proceedings pending in the Opposition Division of the European Patent Office. Final resolution of the opposition proceedings will likely take a number of years. For more information, see Business Intellectual Property.

We are not currently a party to any other material legal proceedings.

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Management

Executive Officers and Directors

Below is a list of the names, ages and positions of the individuals who serve as our executive officers and directors as of March 7, 2014.

Name	Age	Position
John P. Butler	49	President and Chief Executive Officer; Director
Jason A. Amello	45	Senior Vice President, Chief Financial Officer and Treasurer
Robert Shalwitz, M.D.	59	Chief Medical Officer
Nicole R. Hadas	41	Vice President, General Counsel and Secretary
Muneer A. Satter	53	Co-Chairman of the Board of Directors
Campbell Murray, M.D.*	37	Co-Chairman of the Board of Directors
Jack Nielsen	50	Director
Anupam Dalal, M.D.	42	Director
Giovanni Ferrara*	45	Director
Kim Dueholm, Ph.D.	51	Director
Duane Nash, M.D.	43	Director
Michael S. Wyzga	58	Director

* Dr. Murray and Mr. Ferrara resigned immediately prior to the effectiveness of the registration statement of which this prospectus forms a part.

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.

Robert Shalwitz, M.D. co-founded Akebia in 2007. Prior to Akebia, Dr. Shalwitz was Vice President of Clinical Development at Reliant Pharmaceuticals, a biopharmaceutical company, from 2005 to 2007. From 1995 to 2005, Dr. Shalwitz was Medical Director at Abbott Labs. Prior to Abbott Labs, Dr. Shalwitz was an academic pediatric endocrinologist for 10 years, and his research at Washington University in St. Louis and at the Children s Hospital of Orange County (CA) focused on glucose and glycogen metabolism. Dr. Shalwitz received a B.G.S. from

the University of Michigan and an M.D. from SUNY Buffalo.

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Nicole R. Hadas joined Akebia as Vice President, General Counsel and Secretary in 2013. Prior to 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.

Muneer A. Satter has served as a member of our board of directors since 2012. Mr. Satter has been Chairman at Satter Investment Management LLC since 2012. He also manages the Satter Foundation. Prior to Satter Investment Management, Mr. Satter was a partner at Goldman Sachs where he spent 24 years in various roles, most recently as the Global Co-Head of the Principal Debt Group and Global Head of the Mezzanine Group in the Merchant Banking Division. He is Co-Chairman of the Board of Aerpio Therapeutics, Vital Therapies, Inc. and Linq3 Technologies LLC, and Chairman of the Board of Restorsea Holdings, LLC. He also serves as Vice Chairman of Goldman Sachs Foundation and GS Gives, is a director of The Nature Conservancy and World Business Chicago, is on the Board of Advisors of the American Enterprise Institute and is on the Board of Trustees of Northwestern University. Mr. Satter received a B.A. in Economics from Northwestern University, a J.D. from Harvard Law School, and an M.B.A. from Harvard Business School. We believe that Mr. Satter is qualified to serve on our board of directors due to his extensive investment experience.

Campbell Murray, M.D. has served as a member of our board of directors since 2008 and is our Co-Chairman. Dr. Murray has been a Managing Director of Novartis Venture Fund, since 2005. Prior to joining the fund, he worked at the Novartis Institutes for BioMedical Research as the Director of Special Projects. Dr. Murray currently serves on the board of directors of Aerpio Therapeutics, Alios BioPharm, Euthymics Biosciences, Galera Therapeutics, ImaginAb, Neurovance and Tokai Pharmaceuticals. Dr. Murray received a Bachelor of human biology from the University of Auckland Medical School, an M.B.A. from Harvard Business School, an M.P.P. from the John F. Kennedy School of Government, and an MBChB (M.D.) from the University of Auckland Medical School. We believe that Dr. Murray is qualified to serve on our board of directors due to his investment experience in the biotechnology sector.

Jack Nielsen has served as a member of our board of directors since 2013. Mr. Nielsen has worked within the Novo A/S organization and its venture activities since 2001 in several roles, most recently being employed as a Partner based in Copenhagen, Denmark. From 2006 to 2012, Mr. Nielsen was employed as a Partner at Novo Ventures (US) Inc. in San Francisco, where he established the office which provides certain consultancy services to Novo A/S. From 1990-2001, he held various positions in the Novo Nordisk business area which in 2000 became Novozymes A/S. Mr. Nielsen currently serves on the board of directors of Alios BioPharma Inc., Apollo Endosurgery Inc., BioClin Therapeutics Inc., ProteinSimple, Reata Pharmaceuticals Inc. and Tobira Therapeutics Inc. Previously, he was a board member of MediQuest Therapeutics Inc., NeoMend Inc. and Protein Forest Inc. Mr. Nielsen received a M.Sc. in Chemical Engineering from the Technical University in Denmark, and a Master in Management of Technology from Center for Technology, Economics and Management; Technical University of Denmark. We believe that Mr. Nielsen is qualified to serve on our board of directors due to his experience serving on boards in the biotechnology sector.

Anupam Dalal, M.D. has served as a member of our board of directors since 2008. Dr. Dalal has been a managing director at Kearny Venture Partners since 2008. Prior to working at Kearny Venture Partners, Dr. Dalal was a Principal at Flagship Ventures. Dr. Dalal currently serves on the board of directors of Aerpio Therapeutics. Dr. Dalal has served on the board of Resolvyx Pharmaceuticals and Pervasis Therapeutics. Dr. Dalal received a B.A. in Economics from the University of California at Berkley, an M.B.A. from Harvard Business School, and an M.D. from the University of California, San Francisco. Dr. Dalal was Resident in Surgery at Brigham and Women s Hospital / Harvard Medical School. We believe that Dr. Dalal is qualified to serve on our board of directors due to his investment and board experience in the biotechnology sector.

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Giovanni Ferrara has served as a member of our board of directors since 2013. Mr. Ferrara has been a Venture Partner at Novartis Venture Fund since 2011. Prior to joining Novartis, he spent three years as a consultant to west coast venture capital firms and as consulting Chief Business Officer to Sorbent Therapeutics, a biopharmaceutical company. Previously, he was Managing Director and General Partner at Burrill & Company, a venture fund, and began his venture capital career at GeneChem Management, where, in addition to investing, he also held operating positions in portfolio companies, including CEO of Targanta Therapeutics (then Phage Tech, Inc.). Mr. Ferrara received a B.Sc. in Human Genetics and Biology from the University of Toronto, and an M.B.A. and M.Sc. from McGill University. We believe that Mr. Ferrara is qualified to serve on our board of directors due to his management experience in the biotechnology sector.

Kim Dueholm, Ph.D. has served as a member of our board of directors since 2013. Mr. Dueholm has been employed as a partner at Novo A/S since 2000. Prior to joining Novo A/S, Mr. Dueholm spent five years with Novo Nordisk A/S in positions ranging from Patent Portfolio Analyst to Principal Scientific Analyst, from 1995 to 2000. He currently serves on the board of directors of ObsEva SA and Orphazyme ApS. Previously, he was a board member of Core A/S, F-star GmbH, NeuroKey A/S, Novexel S.A., Nuevolution A/S and Symphogen A/S. He is also a member of the editorial board of Expert Opinion on Therapeutic Patents. Mr. Dueholm received an M.Sc. in Chemistry and Business Administration from Odense University, and a Ph.D. in organic chemistry from the University of Copenhagen. We believe that Dr. Dueholm is qualified to serve on our board of directors due to

his management and director experience in the biotechnology sector.

Duane Nash, M.D. has served as a member of our board of directors since 2013. Dr. Nash has been the Executive Vice President since 2013 and Chief Business Officer since 2012 of Vital Therapies, Inc., a biopharmaceutical company. In 2012 and 2013, he also served as Medical Director. Dr. Nash joined Vital Therapies from Wedbush PacGrow Life Sciences, an investment bank, where he was employed from March 2009 to March 2012 serving most recently as Senior Vice President in Equity Research. Before that he was a research analyst at Pacific Growth Equities, an investment bank, from April 2008 through March 2009, which was subsequently acquired by Wedbush Securities, Inc. Dr. Nash also practiced as an attorney from November 2002 to February 2008, most recently at the law firm of Davis Polk, where he focused on intellectual property litigation and corporate matters. Dr. Nash currently serves on the board of directors of Aerpio Therapeutics Inc. Dr. Nash earned a B.A. in biology from Williams College, an M.D. from Dartmouth Medical School, a J.D. from the University of California, Berkeley, and an M.B.A. from the University of Oxford. Dr. Nash completed his internship in general surgery at the University of California at San Francisco. We believe that Dr. Nash is qualified to serve on our board of directors due to his management experience in the biotechnology sector.

Michael S. Wyzga has served as a member of our board of directors since February 2014. Mr. Wyzga has served as the President and Chief Executive Officer and a member of the board of directors of Radius Health, Inc., a biopharmaceutical company focused on developing new therapeutics for the treatment of osteoporosis and other women s health conditions, from December 2011 to November 2013. Prior to that, Mr. Wyzga served in various senior management positions at Genzyme Corporation, a global biotechnology company. Mr. Wyzga joined Genzyme in February 1998 and most recently served as Executive Vice President, Finance from May 2003 until November 2011 and as Chief Financial Officer from July 1999 until November 2011. Mr. Wyzga currently serves on the board of directors of ldenix Pharmaceuticals, Inc., a pharmaceutical company, and Oncomed Pharmaceuticals, Inc., a pharmaceutical company. Mr. Wyzga received a B.S. from Suffolk University and an M.B.A. from Providence College. We believe that Mr. Wyzga is qualified to serve on our board of directors due to his extensive executive and financial leadership.

In addition to the individual attributes of each of our directors listed above, we highly value the collective qualifications and experiences of our board members. We believe the collective viewpoints and perspectives of our directors results in a board that is dedicated to advancing the interests of our stockholders.

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Board Composition and Election of Directors

Board Composition

Our board of directors is currently comprised of seven members. The members of our board of directors were elected in compliance with the provisions of the voting agreement among us and our major stockholders. The voting agreement will terminate upon the closing of this offering and we will have no further contractual obligations regarding the election of our directors. See Certain Relationships and Related Party Transactions. Our directors hold office until their successors have been elected and qualified or until their earlier death, resignation or removal.

Our amended and restated certificate of incorporation and amended and restated bylaws that will become effective upon the closing of this offering provide that the authorized number of directors may be changed only by resolution of our board of directors. Our amended and restated certificate of incorporation and amended and restated bylaws also provide that our directors may be removed only for cause by the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in an annual election of directors, voting together as a single class, at a meeting of the stockholders called for that purpose, and that any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office.

In accordance with the terms of our amended and restated certificate of incorporation that will become effective upon the closing of this offering, our board of directors will be divided into three classes, class I, class II and class III, with members of each class serving staggered three-year terms. Upon the closing of this offering, the members of the classes will be divided as follows:

- the class I directors will be Kim Dueholm and Duane Nash;
- the class II directors will be Anupam Dalal and Jack Nielsen; and
- the class III directors will be John P. Butler, Muneer A. Satter and Michael S. Wyzga.

Upon the expiration of the term of a class of directors, directors in that class will be eligible to be elected for a new three-year term at the annual meeting of stockholders in the year in which their term expires.

We have no formal policy regarding board diversity. Our priority in selection of board members is identification of members who will further the interests of our stockholders through his or her established record of professional accomplishment, the ability to contribute positively to the collaborative culture among board members, knowledge of our business and understanding of the competitive landscape.

Director Independence

Applicable NASDAQ rules require a majority of a listed company s board of directors to be comprised of independent directors within one year of listing. In addition, the NASDAQ rules require that, subject to specified exceptions, each member of a listed company s audit, compensation and nominating and corporate governance committees be independent and that audit committee members also satisfy independence criteria set forth in Rule 10A-3 under the Exchange Act. Under applicable NASDAQ rules, a director will only qualify as an independent director if, in the opinion of the listed company s board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In order to be considered independent for purposes of Rule 10A-3, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors, or any other board committee, accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the listed company or any of its subsidiaries or otherwise be an affiliated person of the listed company or any of its subsidiaries.

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In February 2014, our board of directors undertook a review of the composition of our board of directors and its committees and the independence of each director. Based upon information requested from and provided by each director concerning his or her background, employment and affiliations, including family relationships, our board of directors has determined that Anupam Dalal, Kim Dueholm, Duane Nash, Jack Nielsen, Muneer Satter, and Michael Wyzga are independent directors as defined under applicable NASDAQ rules. In making such determination, our board of directors considered the relationships that each such non-employee director has with our company and all other facts and circumstances that our board of directors deemed relevant in determining his or her independence, including the beneficial ownership of our capital stock by each non-employee director. Mr. Butler is not an independent director under these rules because he is an employee of Akebia. Please see the section of this prospectus titled Certain Relationships and Related Party Transactions.

There are no family relationships among any of our directors or executive officers.

Board Committees

Effective upon the completion of this offering, our board of directors will have three standing committees: the audit committee, the compensation committee and the nominating and corporate governance committee. Our board of directors may establish other committees from time to time.

Audit Committee

Our audit committee consists of Michael Wyzga, Kim Dueholm and Duane Nash, with Michael Wyzga serving as chairman of the committee. Our board of directors has determined that Michael Wyzga and Duane Nash meet the independence requirements of Rule 10A-3 under the Exchange Act and the applicable listing standards of NASDAQ. Our board of directors has determined that Michael Wyzga is an audit committee financial expert within the meaning of the SEC regulations and applicable listing standards of NASDAQ. The audit committee s responsibilities upon completion of this offering will include:

- appointing, approving the compensation of, reviewing the performance of, and assessing the independence of our independent registered public accounting firm;
- pre-approving audit and permissible non-audit services, and the terms of such services, to be provided by our independent registered public accounting firm;
- reviewing the internal audit plan with the independent registered public accounting firm and members of management responsible for preparing our financial statements;
- reviewing and discussing with management and the independent registered public accounting firm our annual and quarterly financial statements and related disclosures as well as critical accounting policies and practices used by us;
- reviewing the adequacy of our internal control over financial reporting;

establishing policies and procedures for the receipt and retention of accounting-related complaints and concerns;

recommending, based upon its review and discussions with management and the independent registered public accounting firm, whether our audited financial statements shall be included in our Annual Report on Form 10-K;

preparing the audit committee report required by the rules of the SEC to be included in our annual proxy statement;

reviewing all related party transactions for potential conflict of interest situations and approving all such transactions; and

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reviewing policies related to risk assessment and risk management; and establishing, maintaining and overseeing our Code of Business Conduct and Ethics.

Compensation Committee

Our compensation committee consists of Anupam Dalal, Jack Nielsen and Muneer Satter, with Anupam Dalal serving as chairman of the committee. Our board of directors has determined that each member of the compensation committee is independent as defined under the applicable listing standards of NASDAQ. The compensation committee s responsibilities upon completion of this offering will include:

annually reviewing and recommending for approval by the independent directors of the board individual and corporate goals and objectives relevant to the compensation of our executive officers;

evaluating the performance of our executive officers in light of such individual and corporate goals and objectives and determining the compensation of our executive officers;

appointing, compensating and overseeing the work of any compensation consultant, legal counsel or other advisor retained by the compensation committee;

conducting the independence assessment outlined in NASDAQ rules with respect to any compensation consultant, legal counsel or other advisor retained by the compensation committee;

annually reviewing and reassessing the adequacy of the committee charter in its compliance with the listing requirements of NASDAQ;

overseeing and administering our compensation and similar plans;

reviewing and approving our policies and procedures for the grant of equity-based awards;

reviewing and making recommendations to the board of directors with respect to director compensation;

reviewing and approving stock option grants, and making recommendations to the board of directors with respect to stock option grants made to directors, executive officers, senior vice presidents or anyone reporting directly to our chief executive officer;

reviewing and discussing with management the compensation discussion and analysis, if any, to be included in our annual proxy statement; and

reviewing and discussing with the board of directors corporate succession plans for the chief executive officer and other senior management positions.

Nominating and Corporate Governance Committee

Our nominating and corporate governance committee consists of Jack Nielsen, Muneer Satter and Michael Wyzga, with Jack Nielsen serving as chairman of the committee. Our board of directors has determined that each member of the nominating and corporate governance committee is independent as defined under the applicable listing standards of NASDAQ. Following this offering, the nominating and corporate governance committee s responsibilities will include:

- developing and recommending to the board of directors criteria for board and committee membership;
- establishing procedures for identifying and evaluating board of director candidates, including nominees recommended by stockholders;
- identifying individuals qualified to become members of the board of directors;
- recommending to the board of directors the persons to be nominated for election as directors and to each of the board s committees; and
- developing and recommending to the board of directors a set of corporate governance principles.

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Compensation Committee Interlocks and Insider Participation

None of our executive officers serves as a member of the board of directors or compensation committee, or other committee serving an equivalent function, of any other entity that has one or more of its executive officers serving as a member of our board of directors or compensation committee. None of the members of our compensation committee has ever been employed by us. For a description of transactions between us and members of our compensation committee and affiliates of such members, please see the section of this prospectus titled Certain Relationships and Related Party Transactions.

Code of Business Conduct and Ethics

We have adopted a code of business conduct and ethics that applies to all of our employees, officers and directors, including those officers responsible for financial reporting. Upon the closing of this offering, our code of business conduct and ethics will be available on our website. We intend to disclose amendments to the code, or any waivers of its requirements, on our website as may be required by law or NASDAQ stock market listing standards.

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Executive Compensation

This section discusses the material elements of our executive compensation policies and decisions and important factors relevant to an analysis of these policies and decisions. It provides qualitative information regarding the manner and context in which compensation is awarded to and earned by our executive officers named in the Summary Compensation Table below and is intended to place in perspective the information presented in the following tables and the corresponding narrative.

Overview

Historically, our executive compensation program has reflected our growth and corporate goals. To date, the compensation of our executive officers has consisted of a combination of base salary, annual cash bonus, long-term equity incentive compensation in the form of restricted stock and stock options and other employee benefits generally available to our employees. Certain of our executive officers are also entitled to certain compensation and benefits upon certain terminations of employment. Prior to March 3, 2014, these rights were determined pursuant to their employment agreements, as described below. Effective as of March 3, 2014, the rights of our executive officers to compensation and benefits upon a termination of employment will be determined pursuant to their executive severance agreements, as described below.

Our named executive officers for the year ended December 31, 2013 were as follows:

- John P. Butler, our President and Chief Executive Officer;
- Joseph Gardner, Ph.D., our former President and Chief Executive Officer;
- Robert Shalwitz, M.D., our Chief Medical Officer; and
- William Daly, our former Chief Business Officer.

John P. Butler was hired as our President and Chief Executive Officer in September 2013 and appointed as a member of our board of directors effective July 2013. In connection with Mr. Butler s appointment, Dr. Gardner resigned as President and Chief Executive Officer and as a member of our board of directors, although he continues to serve as a consultant to the Company.

We and William Daly mutually agreed to terminate Mr. Daly s employment effective as of February 7, 2014, although he continues to serve as a consultant to the Company, all as described in more detail below under Employment Agreements with Our Named Executive Officers.

Elements of Executive Compensation

Base Salaries. Base salaries for our named executive officers are determined annually by our compensation committee, subject to review and approval by our board of directors, based on the scope of each officer s responsibilities along with his respective experience and contributions to the company during the prior year period. When reviewing base salaries, our compensation committee takes factors into account such as each officer s experience and individual performance, the company s performance as a whole, data from surveys of compensation paid by comparable companies, and general industry conditions, but does not assign any specific weighting to any factor.

Annual Cash Bonuses. Our annual cash bonus program promotes and rewards our executives for the achievement of key strategic and business goals. The bonus plan period has historically covered the twelve consecutive month period ending each June 30. For 2013, we decided to change the bonus plan period to a calendar year period ending each December 31. As a result, the 2013 bonus plan period covers the 18-month period beginning on July 1, 2012 and ending on December 31, 2013. For the 2013 bonus plan period, the target annual bonus as a percentage of base salary (as determined based on the salary earned throughout the bonus plan period) for each of Mr. Butler, Dr. Shalwitz, and Mr. Daly was 30%, 20% and 20%, respectively. At the beginning of the 2013 bonus plan period, our compensation committee established corporate performance goals, each having a designated weighting, that related to key development, strategic and financial goals of the company**.** At the end of the 2013 bonus plan period, our compensation committee met and evaluated the performance of the company against the specified performance goals. For Mr. Daly and Dr. Shalwitz, the payout is dependent in part upon the

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achievement of specified performance goals for Aerpio. The portion of the payout that is dependent on those goals is determined by reference to the amount of time spent by the executive officer on Aerpio matters (5% for Dr. Shalwitz and 30% for Mr. Daly). Based on its evaluation, the compensation committee recommended and the board of directors approved, payment of cash bonuses for the 2013 bonus plan period of: $37,188 for Mr. Butler (which represented 100% of his target bonus, as prorated to reflect his commencement of employment in September 2013), $59,863 for Dr. Shalwitz (which represented 72% of his target bonus), and $40,165 to Mr. Daly (which represented 50% of his target bonus). Due to other benefits provided to Dr. Gardner in connection with his Separation Agreement, Dr. Gardner did not receive a cash bonus for the 2013 bonus plan period.

Equity Awards. Our named executive officers participate in our Akebia Therapeutics, Inc. 2008 Equity Incentive Plan, or the 2008 Equity Incentive Plan. During fiscal 2013, Mr. Butler received a grant of stock options, Dr. Gardner and Dr. Shalwitz received a grant of restricted stock and Mr. Daly received grants of stock options and restricted stock. These stock option and restricted stock grants are subject to time-based vesting conditions and generally vest, subject to continued employment, as to 25% of the shares subject to the award after one year and thereafter continue to vest in quarterly installments over the following three years. These equity awards serve to align the interests of our named executive officers with our shareholders. They also encourage retention through the use of time-based vesting. For more information regarding the awards granted under the 2008 Equity Incentive Plan, please refer to Equity Incentive Plans *2008 Equity Incentive Plan* below.

Benefits. Our named executive officers are eligible for benefits, such as participation in our 401(k) plan and basic health and welfare benefit coverage, that are generally available to all of our employees.

Summary Compensation Table

The following table sets forth information regarding compensation awarded to, earned by or paid to each of our named executive officers during the fiscal years ending December 31, 2013 and 2012.

Summary Compensation Table

Name and Principal Position	Year	Salary ($)	Bonus ($)[1]	Stock Awards ($)[2]	Option Awards ($)[3]	All Other Compensation ($)	Total ($)
John P. Butler	2013	124,802[5]	37,188		2,126,887	40[4]	2,288,917
President and Chief Executive Officer							
Joseph Gardner, Ph.D.	2013	203,472[8]		1,068,100[12]	50,317[13]	28,530[6]	1,350,419
Former President and Chief Executive Officer	2012	275,000	36,438		44,546	251[4]	356,235
Robert Shalwitz, M.D.	2013	294,140[9]	59,863	943,983		24,982[7]	1,322,968
Chief Medical Officer	2012	269,280	31,680		6,126	455[4]	307,541
William Daly	2013	289,583[10]	40,165	47,990	523,024	697[4]	901,459
Senior Vice President, Business Development	2012	259,375[11]	20,625	57,089		455[4]	337,544

(1) Amounts for 2013 represent cash bonuses earned for the 18-month bonus plan period from July 1, 2012 to December 31, 2013. Amounts for 2012 represent cash bonuses earned for the 12-month bonus plan period from July 1, 2011 to June 30, 2012.

(2) The amount reported in the Stock Awards column granted to our named executive officers represents the retrospective fair value of the stock awards as of the grant date in accordance with ASC, Topic 718.

(3) The amounts reported in the Option Awards column granted to our named executive officers represent the retrospective fair value of the stock options as of the grant date as computed in

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accordance with Accounting Standards Codification, or ASC, Topic 718, not including any estimates of forfeitures. The assumptions used in calculating the grant date fair value of the stock options reported in the Option awards column are set forth in Note 12 to our consolidated financial statements included elsewhere in this prospectus. Note that the amounts reported in this column reflect the accounting cost for these stock options, and do not correspond to the actual economic value that may be received by the named executive officers from the options.

(4) Amounts represent the dollar value of life insurance premiums paid by the company on behalf of the named executive officer.

(5) Mr. Butler joined us in September 2013. Mr. Butler s annual base salary in 2013 was $425,000. The amounts in the table above reflect his partial year of service in 2013.

(6) Amounts include: (i) $522 for the dollar value of life insurance premiums paid by the company and (ii) forgiveness of principal on a portion of promissory notes to the company in the amount of $28,008. See Note 12 under *2013 Outstanding Equity Awards at Fiscal Year-End*.

(7) Amounts include: (i) $696 for the dollar value of life insurance premiums paid by the company and (ii) forgiveness of principal on a portion of promissory notes to the company in the amount of $24,286. See Note 12 under *2013 Outstanding Equity Awards at Fiscal Year-End*.

(8) Dr. Gardner s annual base salary was $275,000 from January 2013 through July 2013, and was $350,000 beginning August 1, 2013. Dr. Gardner resigned as President and Chief Executive Officer and as a member of our board of directors on September 15, 2013. The amounts in the table above reflect his partial year of service in 2013.

(9) Dr. Shalwitz s annual base salary was $269,280 from January 2013 through July 2013, and was $330,000 beginning August 1, 2013.

(10) Mr. Daly s annual base salary was $275,000 from January 2013 through July 2013, and was $310,000 beginning August 1, 2013. The Company and William Daly mutually agreed to terminate Mr. Daly s employment effective as of February 7, 2014, although he continues to serve as a consultant to the Company.

(11) Mr. Daly joined us in January 2012. Mr. Daly s annual base salary in 2012 was $275,000. The amounts in the table above reflect his partial year of service in 2012.

(12) Amount represents the fair value of the following awards at the grant dates: (1) 37,108 shares granted pursuant to the separation agreement described in Employment Agreements with Our Named Executive Officers below and 105,753 shares granted following Mr. Gardner s resignation, in each case in consideration of his prior service as our President and Chief Executive Officer and (2) 33,947 shares granted pursuant to the consulting agreement described in Employment Agreements with Our Named Executive Officers below, as compensation for services to be performed in his new role as consultant to the Company. The amount also includes $15,100 associated with the accelerated vesting of restricted stock pursuant to Dr. Gardner s Separation Agreement.

(13) Amount represents the value associated with accelerated vesting of stock options pursuant to Dr. Gardner s Separation Agreement.

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2013 Outstanding Equity Awards at Fiscal Year-End

The following table sets forth information concerning outstanding equity awards for each of our named executive officers at December 31, 2013:

	Stock Options				Stock Awards[11]	
Name and Principal Position	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Option Exercise Price ($)	Option Expiration Date	Number of Shares or Units of Stock That Have Not Vested (#)	Market Value of Shares of Stock That Have Not Vested ($)[10]
John P. Butler. . . . . *President and Chief Executive Officer*		612,500[1]	$ 0.47	9/16/2023		
Joseph Gardner, Ph.D. *Former President and Chief Executive Officer*		[2]			[2]	
Robert Shalwitz, M.D.	66,551		$ 0.86	6/1/2018		
Chief Medical Officer	26,012	4,321[3]	$ 0.86	7/28/2020	13,078[6]	97,074
	9,454	9,223[4]	$ 0.86	1/12/2022	127,173[7]	943,983
William Daly					27,388[8]	203,924
Senior Vice President, Business Development		90,472[5]	$ 3.77	12/23/2023	53,835[9]	399,611

(1) Represents options to purchase shares of our common stock granted on September 16, 2013. The remaining unvested shares will vest as follows: 25% vest on September 16, 2014, with the remainder of the shares vesting in equal monthly installments over the following three years through September 16, 2017. Vesting of all unvested options shall accelerate in connection with an acquisition event pursuant to the terms of the option agreement.

(2) In connection with Dr. Gardner s resignation as President and Chief Executive Officer and as a member of our board of directors, all of Dr. Gardner s outstanding equity awards were accelerated and became fully vested as of September 15, 2013 pursuant to his Separation Agreement. Following his separation, 136,855 options with a weighted-average exercise price of $0.86 per share expired unexercised.

(3) Represents options to purchase shares of our common stock granted on July 28, 2010. The remainder of these options vests in equal monthly installments through July 28, 2014. Vesting of all unvested options shall accelerate in connection with an acquisition event pursuant to the terms of the option agreement.

(4) Represents options to purchase shares of our common stock granted on January 12, 2012. The remainder of these options vests in equal monthly installments through December 23, 2015. Pursuant to the terms of the award agreement, vesting of all unvested options shall accelerate in connection with an acquisition, in the event the option is not assumed by the acquirer, or in the event the option is assumed by the acquirer and the executive s employment is terminated or materially diminished within the following 12 months.

(5) Represents options to purchase shares of our common stock granted on December 23, 2013. Prior to cancellation, the remaining unvested shares were scheduled to vest as follows: 25% vest on April 1, 2014, with the remainder of the shares vesting in equal monthly installments over the following three years through April 1, 2017, with vesting of all unvested options accelerating in connection with an acquisition event pursuant to the terms of the option agreement; provided that no shares would vest prior to the occurrence of a liquidity event. All of these options were cancelled pursuant to the Separation Agreement between us and Mr. Daly, as described below.

(6) Under the terms of the June 15, 2011 restricted stock agreement, the remaining unvested shares will vest in equal monthly installments through April 6, 2015. Vesting of all restricted shares shall accelerate in connection with an acquisition event pursuant to the terms of the restricted stock agreement.

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(7) Under the terms of the December 23, 2013 restricted stock agreement, the remaining unvested shares will vest as follows: 25% vest on December 23, 2014, with the remainder of the shares vesting in equal quarterly installments over the following three years through December 23, 2017; provided that no shares or restricted stock would vest prior to the occurrence of a liquidity event. Vesting of all restricted shares shall accelerate in connection with an acquisition event pursuant to the terms of the restricted stock agreement.

(8) Under the terms of the February 21, 2012 restricted stock agreement: 25% vested on January 22, 2013, with the remainder of the unvested shares vesting in equal monthly installments over the following three years through January 22, 2016. Pursuant to the terms of the award agreement, vesting of all unvested shares shall accelerate in connection with an acquisition, in the event the award is not assumed by the acquirer, or in the event the award is assumed by the acquirer and the executive s employment is terminated or materially diminished within the following 12 months. The vesting schedule for these shares was revised pursuant to the Separation Agreement and the Consulting Agreement between us and Mr. Daly, as described below.

(9) Prior to cancellation, under the terms of the April 1, 2013 restricted stock agreement, the remaining unvested shares were scheduled to vest as follows: 25% vest on April 1, 2014, with the remainder of the shares vesting in equal monthly installments over the following three years through April 1, 2017 and vesting of all unvested shares shall accelerate in connection with an acquisition, in the event the award is not assumed by the acquirer, or in the event the award is assumed by the acquirer and the executive s employment is terminated or materially diminished within the following 12 months. All of these shares of restricted stock were cancelled pursuant to the Separation Agreement between us and Mr. Daly, as described below.

(10) The value of the unvested restricted stock was $7.42 per share based on an independent, third-party appraisal of our common stock as of December 31, 2013.

(11) The restricted stock awards for Dr. Gardner and Dr. Shalwitz were purchased using promissory notes issued by the executives to the Company (the Promissory Notes) for $140,884 and $110,692, respectively. The Promissory Notes were amended in 2013 to forgive a portion of the principal owed and to reduce the interest rate from 6% to 3% per annum. The aggregate balance of the outstanding Promissory Notes at December 31, 2013 was $112,831 for Dr. Gardner and $86,406 for Dr. Shalwitz. The Promissory Notes are repayable at the earlier of (a) an initial public offering; (b) the sale of the company or substantially all of its assets; (c) the termination of the employee; or (d) five years from origination. Dr. Shalwitz s note, including accrued interest in the aggregate amount of $88,072, was forgiven on January 30, 2014.

Retention Bonuses

We have established a retention bonus program in which our named executive officers participate. This program provides that if the named executive officers remain employed with us through a Sale of the Company (as defined in the Third Amended and Restated Voting Agreement), they will be paid a bonus in the same form and manner as payments made to holders of our Series C Preferred Stock in connection with the Sale of the Company . Each participant in the program is entitled to a designated percentage of a bonus pool. The designated percentages have not yet been determined and no awards have been made pursuant to this program. The size of the bonus pool is based on (i) the percentage of our fully-diluted equity that is represented by vested awards under our 2008 Equity Incentive Plan immediately prior to a Sale of the Company (up to a maximum of 12.5%) multiplied by (ii) fifty percent of the Applicable Accrued Value (as defined in our eighth amended and restated certificate of incorporation) of our Series C Preferred Stock. We do not expect to maintain the retention bonus program following the consummation of this offering.

Retirement Benefits

We offer a tax-qualified retirement plan, or 401(k) plan, to eligible employees, including our named executive officers. In accordance with this plan, all eligible employees may 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 2013 or 2012.

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Employment Agreements with Our Named Executive Officers

We have entered into an employment agreement with each of our named executive officers, except for Mr. Daly, with whom we entered into an offer letter at the time he commenced employment with us. Each of these employment agreements and offer letter provides for at will employment, meaning that either we or the named executive officer may terminate our employment relationship at any time without cause.

John P. Butler. On September 16, 2013, we entered into an executive employment agreement with Mr. Butler for the position of President and Chief Executive Officer. The executive employment agreement continues until we or Mr. Butler terminates the agreement in accordance with its terms. Mr. Butler currently receives a base salary of $425,000, which is subject to review by our Board of Directors from time to time, and at least every 12 months. Mr. Butler is also eligible to receive an annual performance-based cash bonus of up to 30% of Mr. Butler s base salary, determined by our board of directors and based upon the company s performance and Mr. Butler s performance against objectives established by our board of directors. Mr. Butler is entitled to four weeks of vacation, as well as holidays and sick leave, and (subject to eligibility criteria under the applicable plan) the right to participate in any profit sharing plan, retirement plan, 401(k) plan, group medical plan, group dental plan, and/or other health or insurance plan maintained by us for our senior executives generally and, if applicable, their family members. Mr. Butler is also entitled to reimbursement of all reasonable and necessary business and travel expenses incurred in connection with the performance of his duties.

Dr. Joseph Gardner. On May 2, 2007, we entered into an executive employment agreement with Dr. Gardner for the position of President and CEO; this agreement was subsequently amended on April 6, 2011. Dr. Gardner s base salary during 2013 was $350,000, which was subject to review by our Board of Directors from time to time during his employment, and at least every 12 months. Dr. Gardner was also eligible to participate in discretionary bonus programs on both a quarterly and annual basis, as determined by our Board of Directors, in its sole discretion; provided; that Dr. Gardner was not entitled to payment of any such bonus unless he remained actively employed through the end of the applicable calendar quarter or year. Dr. Gardner was entitled to four weeks of vacation, as well as holidays and sick leave, and (subject to eligibility criteria under the applicable plan) the right to participate in any profit sharing plan, retirement plan, 401(k) plan, group medical plan, group dental plan, and/or other health or insurance plan maintained by us for our senior executives generally and, if applicable, their family members. Dr. Gardner was also entitled to reimbursement of all reasonable and necessary business and travel expenses incurred in connection with the performance of his duties. Dr. Gardner resigned as President and CEO in September 2013. He continues to serve as a consultant. Although Dr. Gardner was not entitled to any severance under his employment agreement upon his termination of employment, we entered into a separation agreement with him that provided for the accelerated vesting of all his then unvested options and restricted stock. The separation agreement also provided Dr. Gardner with an award of 37,018 shares of unrestricted common stock, without consideration therefor, and stated that Dr. Gardner would participate in the retention bonuses described above. The separation agreement also contained a release of claims in favor of the company. Concurrent with the separation agreement, we entered into a standard consulting agreement with Dr. Gardner pursuant to which we granted him 33,947 unrestricted shares of our common stock.

Dr. Robert Shalwitz. On April 6, 2011, we entered into an executive employment agreement with Dr. Shalwitz for the position of Chief Medical Officer and Vice President. Dr. Shalwitz currently receives a base salary of $330,000, which is subject to review by our Board of Directors from time to time, and at least every 12 months. Dr. Shalwitz is also eligible to participate in all bonus or similar incentive plans adopted by our Board of Directors including, without limitation, an incentive compensation plan with a yearly performance-based cash bonus of up to 20% of Dr. Shalwitz s base salary. Dr. Shalwitz is entitled to four weeks of vacation, as well as holidays and sick leave, and (subject to eligibility criteria under the applicable plan) the right to participate in any profit sharing plan, retirement plan, 401(k) plan, group medical plan, group dental plan, and/or other health or insurance plan maintained by us for our senior executives generally and, if applicable, their family members. We pay 100% of Dr. Shalwitz s premiums under our medical and dental plans and 50% of the premiums associated with the coverage of his spouses/dependents under those same plans. Dr. Shalwitz is also entitled to reimbursement of all reasonable and necessary business and travel expenses incurred in connection with the performance of his duties.

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Mr. William Daly. On January 2, 2012, we entered into an offer letter with Mr. Daly for the position of Senior Vice President of Business Development. Under the offer letter, Mr. Daly received an annual base salary of $310,000 and was eligible for performance-based cash bonuses of up to a maximum of 20% of base salary per year. Mr. Daly s offer letter also entitled him to an initial grant of restricted stock under our 2008 Equity Incentive Plan, subject to approval by our board of directors. For more information about the restricted stock grant made to Mr. Daly upon the commencement of his employment in 2012, please see the 2013 Outstanding Equity Awards at Fiscal Year-End table above. Mr. Daly s base salary and incentive compensation were subject to review on an annual basis. Mr. Daly was entitled to participate in all benefit plans as may have been offered by us from time to time during his employment. We and Mr. Daly mutually agreed to terminate Mr. Daly s employment effective as of February 7, 2014. In connection with his resignation, we and Mr. Daly entered into a Separation Agreement and Consulting Agreement. Under the Separation Agreement, Mr. Daly is entitled to twelve months of salary continuation (in an aggregate amount of $310,000) and payment of a portion of his COBRA premiums for a maximum of twelve months (on the same basis as the medical insurance premium paid by us during his employment), as well as a reimbursement of up to $5,000 for legal fees incurred. In addition, the Separation Agreement provides for the following treatment of Mr. Daly s outstanding equity incentive awards: (i) the cancellation, without consideration therefor, of 90,472 stock options granted on December 23, 2013 and 53,835 shares of restricted stock granted on April 1, 2013 and (ii) the continued vesting of 52,582 shares of restricted stock granted on February 21, 2012 during the twelve month period following his separation, with any remaining unvested portion of this restricted stock award vesting on the last day of such twelve month period or, if earlier, upon a change of control of the company (as defined in the consulting agreement) or the termination of the Consulting Agreement by us without cause (as defined in the consulting agreement). Our obligation to provide Mr. Daly with these severance benefits, including the continued vesting of his February 21, 2012 restricted stock award, is conditioned on his continued compliance with the terms of the Consulting Agreement and the Separation Agreement, including the restrictive covenants described below. The Separation Agreement also includes a general release from any liability related to the employment and termination of Mr. Daly.

Under Mr. Daly s Consulting Agreement, he will continue, for a twelve-month period following February 7, 2014, to advise us with respect to, among other things, our business development activities and intellectual property portfolio. As consideration for the performance of these services and his continuing obligation to abide by certain restrictive covenants related to non-competition, non-solicitation and confidentiality, the Consulting Agreement provides Mr. Daly with a grant of 56,000 shares of restricted stock and a $150,000 payment to partially offset a valid Code section 83(b) election. Half of this restricted stock grant vests on the six-month anniversary of the Consulting Agreement, with the remainder vesting on the expiration of the Consulting Agreement or, if earlier, upon a change of control of the company (as defined in the Consulting Agreement) or the termination of the consulting agreement by us without cause (as defined in the Consulting Agreement). If Mr. Daly terminates the consulting agreement for convenience or we terminate it for cause (as defined in the Consulting Agreement), then the vesting of all equity (i.e., the February 21, 2012 restricted stock award and the 56,000 shares of restricted stock provided in consideration for his consulting services) and the payment of all severance and benefits under the Consulting Agreement and the Separation Agreement shall cease.

Involuntary Termination of Employment and Change of Control

Pursuant to their employment agreements, Mr. Butler, Dr. Gardner and Dr. Shalwitz are eligible to receive certain payments and benefits in the event that the executive s employment is terminated by us without cause (as defined in the applicable employment agreement), the executive terminates his employment with us for good reason (as defined in the applicable employment agreement) or, with respect to Dr. Gardner and Dr. Shalwitz (but not Mr. Butler), the executive is terminated in connection with or within six months following a change of control (as defined in the applicable employment agreement). As described below, effective as of March 3, 2014, we entered into a new executive severance agreement with each of Mr. Butler and Dr. Shalwitz. These executive severance agreements supersede the provisions regarding post-separation severance and benefits and equity acceleration in connection with a change of control included in Mr. Butler s and Dr. Shalwitz s employment agreements, which otherwise remain in effect in accordance with their terms. From and after

March 3, 2014, the rights of Mr. Butler and Dr. Shalwitz to any payments or benefits following a termination of employment will be determined under the executive severance agreements described below.

Under their employment agreements, the severance payable to Dr. Gardner and Dr. Shalwitz in each applicable situation, which is subject in all cases to the execution of a release of claims in our favor and continued compliance with a set of restrictive covenants prohibiting certain competitive behaviors by the executive within the one-year period immediately following his termination of employment, is equal to six months of salary continuation, the Company s payment of the executive s COBRA premiums for a maximum of six months, and six months of participation in our group insurance benefits (other than health insurance) in which the executive participated immediately prior to termination. As noted above, Dr. Gardner resigned as President and CEO on September 15, 2013. Except as described above, no severance was or is payable to Dr. Gardner under his employment agreement in connection with this termination of employment.

Under his employment agreement, the severance payable to Mr. Butler in each applicable situation, which is subject in all cases to the execution of a release of claims in our favor and continued compliance with a set of restrictive covenants prohibiting certain competitive behaviors by Mr. Butler within the one-year period immediately following his termination of employment, is equal to twelve months of salary continuation and the Company s payment of Mr. Butler s COBRA premiums for a maximum of twelve months. In addition, Mr. Butler is entitled to receive a pro-rata portion of his annual target bonus for the calendar year in which his termination of employment occurs.

Executive Severance Agreements

On February 28, 2014, our board of directors adopted a form of executive severance agreement, or ESA, under which our officers, including our named executive officers, are eligible to receive certain payments and benefits in the event that the executive s employment with us is terminated without cause, the executive terminates his or her employment with us for good reason, or the executive is terminated in connection with or within 12 months after a change in control (each as defined in the ESA). The ESAs also provide for accelerated vesting of outstanding and unvested equity awards upon a change in control (as defined in the ESA). Effective as of March 3, 2014, we entered into ESAs with Mr. Butler and Dr. Shalwitz. The terms of the ESAs with Mr. Butler and Dr. Shalwitz supersede the terms of all existing agreements between us and such executives regarding post-separation severance and benefits and equity acceleration in connection with a change of control, including any such terms in the severance provisions of each of their employment agreements, as described above, and any such terms in any outstanding equity award. All other terms of any existing agreement between such executives and us, such as the terms of their existing employment agreements related to compensation and benefits during employment, will otherwise remain in full force and effect in accordance with the terms of such existing agreements.

Termination of Employment without Cause or for Good Reason. Under the ESA, if Mr. Butler s or Dr. Shalwitz s employment is terminated by us without cause or the executive terminates his employment for good reason (each as defined in the ESA), other than following a change in control as described below, the executive will be entitled to receive, in addition to any amounts earned or accrued but unpaid as of the date of termination, 12 months of salary continuation and up to 12 months of reimbursement of a portion of the executive s health and dental COBRA premiums to the same extent as if the executive remained employed. In addition, the executive s unvested equity and equity-based awards will remain outstanding and continue to vest in accordance with their terms during the executive s severance period, as if he had remained employed during that time.

Termination of Employment without Cause or for Good Reason Following a Change in Control. If, within 12 months following a change in control (as defined in the ESA), Mr. Butler s or Dr. Shalwitz s employment is terminated by us without cause or the executive terminates his employment for good reason (each as defined in the ESA), the executive will be entitled to receive, in addition to any amounts earned or accrued but unpaid as of the date of termination, 12 months of salary continuation, up to 12 months of reimbursement of a portion of the executive s health and dental COBRA premiums to the same extent as if the executive remained employed, and an

amount equal to fifty percent (50%) of the executive s annual target bonus for the year of termination, prorated based on the number of months the executive was employed during the year prior to termination. In addition, the executive s unvested equity and equity-based awards will remain outstanding and continue to vest in accordance with their terms during the executive s severance period, as of he had remained employed during that time.

Conditions to the Receipt of Severance Benefits. The severance payments and benefits described above are conditioned upon Mr. Butler s or Dr. Shalwitz s execution of a general release of claims in our favor and continued compliance with a set of restrictive covenants prohibiting certain competitive behaviors following termination and a prohibition on making certain statements that are disparaging about or adverse to our business interests or that are otherwise intended to harm our reputation for at least one year following termination. In addition, we may terminate severance payments to either Mr. Butler or Dr. Shalwitz if, within one year following a termination without cause, we determine that the Company had the right to terminate his employment for cause.

Accelerated Vesting of Equity upon a Change in Control. Under the ESA, 100% of each of Mr. Butler s and Dr. Shalwitz s outstanding and unvested equity and equity-based awards will become immediately vested upon a change in control, (as defined in the ESA) irrespective of whether his employment terminates in connection with the change in control.

Other Termination of Employment. If Mr. Butler s or Dr. Shalwitz s employment is terminated for any reason other than by us without cause or by the executive for good reason (including by reason of death or disability), the executive will only be entitled to receive any amounts earned or accrued but unpaid as of the date of termination in accordance with our normal policies and practices, including any salary, bonus or incentive compensation with respect to the calendar year prior to the year of termination, business expenses incurred in the performance of the executive s duties, and vacation pay.

280G Cutback. All payments to Mr. Butler or Dr. Shalwitz under the ESA, including, without limitation, the payment of severance benefits or the accelerated vesting of equity, will be reduced or adjusted to avoid triggering the excise tax imposed by Section 4999 of the Code, if such adjustment would result in the provision of a greater total benefit, on a net after-tax basis (after taking into account taking any applicable federal, state and local income taxes and the excise tax imposed by Section 4999), to the executive.

Termination of ESA. Each of Mr. Butler s and Dr. Shalwitz s ESA will terminate immediately upon the mutual agreement of the parties to such ESA, the executive s termination for cause or death, or the executive s disability (defined as the executive s inability by reason of physical or mental impairment to perform his job duties for a period exceeding twelve (12) consecutive weeks).

Equity Incentive Plans

All outstanding equity-based awards have been granted under our 2008 Equity Incentive Plan, as described below. Following this offering, all equity-based awards will be granted under the 2014 Incentive Plan described below.

2008 Equity Incentive Plan

Our Board of Directors and shareholders originally approved the 2008 Equity Incentive Plan, effective as of April 4, 2008. The following summary describes the material terms of the 2008 Equity Incentive Plan, as most recently amended effective August 3, 2013. This summary of the 2008 Equity Incentive Plan is not a complete description of all provisions of the 2008 Equity Incentive Plan and is qualified in its entirety by reference to the 2008 Equity Incentive Plan, which will be filed as an exhibit to the registration statement of which this prospectus is a part.

Administration. The 2008 Equity Incentive Plan is administered by our Board of Directors. Our Board of Directors has the authority to, among other things, determine to which of the eligible persons under the plan

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awards will be granted, determine the type of award to grant, approve forms of award agreements, determine the number of shares subject to, and the terms and conditions of, an award, construe and interpret the plan and awards and establish, amend and revoke rules and regulations for the administration of the plan and awards, correct defects in the plan and awards and generally, to exercise such powers and perform such acts as it deems to be necessary or expedient to make the plan fully effective. Our Board of Directors determinations under the 2008 Equity Incentive Plan are final and conclusive.

Eligibility. Our employees, directors, and consultants are eligible to participate in the 2008 Equity Incentive Plan. Eligibility for stock options intended to be incentive stock options, or ISOs, as defined in Section 422 of the Code, is limited to our employees.

Authorized Shares. Subject to adjustment, as described below, as of January 24, 2014, the number of shares of our common stock reserved for future issuance under the 2008 Equity Incentive Plan is 155,108 shares. The shares of our common stock to be issued under the 2008 Equity Incentive Plan may be authorized but unissued shares of our common stock or previously issued shares of our common stock acquired by us. Any shares of our common stock underlying awards that are settled in cash, forfeited, repurchased or otherwise reacquired by us, expired, cancelled or become unexercisable without having been exercised and any shares of our common stock used to satisfy an applicable tax withholding obligation will again be available for issuance under the 2008 Equity Incentive Plan.

Types of Awards. The 2008 Equity Incentive Plan provides for awards of stock options, restricted stock and unrestricted stock.

Stock options. The exercise price of an ISO may not be less than the fair market value (or, in the case of an ISO granted to a ten percent shareholder, 110% of the fair market value) of shares of our common stock on the date of grant. The exercise price of each non-statutory stock option (or NSO) is the exercise price determined by our Board of Directors. The Board of Directors has set the exercise price of all NSOs granted under the 2008 Equity Incentive Plan at the fair market value of shares of our comment stock as of the actual date of grant. Our Board of Directors will determine the time or times at which stock options become exercisable and the terms on which such awards remain exercisable.

Restricted stock and stock bonuses. A restricted stock award is an award of shares of our common stock subject to forfeiture restrictions. A stock bonus is not subject to such restrictions. Our Board of Directors will determine the time or times at which any applicable vesting conditions and/or repurchase rights on restricted and unrestricted stock awards will lapse.

Vesting; Termination of Employment or Service. Our Board of Directors has the authority to determine the vesting schedule applicable to each award, and to accelerate the vesting or exercisability of any award. In the case of stock options, our Board of Directors may provide for early exercise of unvested options, with the stock received upon such exercise being subject to vesting. Our Board of Directors will determine the effect of termination of employment or service on an award. Unless otherwise provided in an award agreement, upon a termination of a participant s employment or service, all unvested stock options held by the participant on the date notice of termination is given to the optionee will terminate and all other unvested awards will be forfeited and all vested stock options then held by the participant will remain outstanding for one month following the provision of notice of such termination, or, in the case of death or disability, one year following the date of death or the provision of notice of termination by reason of disability or, in each case, until the applicable expiration date, if earlier. All stock options held by a participant immediately prior to the participant s termination of employment or service will immediately terminate if such termination is for cause, as defined in the 2008 Equity Incentive Plan. Unless otherwise provided by our Board of Directors, a stock bonus or restricted stock award shall cease vesting upon a participant s termination of employment or service (and, if applicable, the right to acquire any stock purchasable under such award will cease).

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Non-Transferability of Awards. Awards under the 2008 Equity Incentive Plan may not be transferred other than by will or by the laws of descent and distribution, unless, for awards other than ISOs, otherwise provided in an award agreement (and subject, in the case of restricted stock and unrestricted stock awards to any applicable buy-sell or similar arrangements).

280G cutback. If any payment or right accruing to an individual under the 2008 Equity Incentive Plan would (alone or together with any other payment or right) constitute a parachute payment for purposes of Section 280G of the Code, then such payment or right under the 2008 Equity Incentive Plan will be reduced to the largest amount or greatest right that will result in no portion of such payment or right being a parachute payment . This provision will only apply if the individual would receive less on an after tax basis if he or she did not have his or her payment or right under the 2008 Equity Incentive Plan so reduced.

Certain Transactions; Certain Adjustments. In the event of a merger, consolidation, reorganization, recapitalization, reincorporation, stock dividend, dividend in property other than cash, stock split, liquidating dividend, combination of shares, exchange of shares, change in corporate structure or other transaction not involving the receipt of consideration by the corporation, the Board of Directors will appropriately adjust the maximum number of shares that can be issued under the 2008 Equity Incentive Plan, as well as all outstanding awards, except that no adjustment will be made if it would cause an equity award intended to be an ISO to fail to so qualify.

In the event of a deemed liquidity event (as defined in our certificate of incorporation), our Board of Directors may provide for substitute awards or such alternative consideration, including cash, as it deems equitable in the situation. In the event that our Board of Directors does not provide for such substitution or consideration in connection with a covered transaction, except as otherwise provided in an award agreement, all unexercised options will terminate automatically and, in the case of outstanding unvested restricted stock or stock bonus awards, will be forfeited automatically (in exchange for an amount equal to the original purchase price, if any) upon the consummation of such covered transaction. No additional awards may be made under the 2008 Equity Incentive Plan following a covered transaction.

Amendment; Termination. Our Board of Directors may, in its discretion, amend the 2008 Equity Incentive Plan or suspend or terminate the 2008 Equity Incentive Plan at any time, except that our Board of Directors may not reduce any outstanding award without the participant s written consent. Shareholder approval will be required for any amendment to the 2008 Equity Incentive Plan to the extent such approval is required by law. Unless earlier terminated by our Board of Directors, the 2008 Equity Incentive Plan will terminate by its terms on April 3, 2018.

2014 Incentive Plan

On February 28, 2014, our board of directors adopted the Akebia Therapeutics, Inc. 2014 Incentive Plan, or the 2014 Incentive Plan, and, following this offering, all equity-based awards will be granted under the 2014 Incentive Plan. As of the date of this prospectus, no awards have been made under the 2014 Incentive Plan. The following summary describes the material terms of the 2014 Incentive Plan. This summary of the 2014 Incentive Plan is not a complete description of all provisions of the 2014 Incentive Plan and is qualified in its entirety by reference to the 2014 Incentive Plan, which will be filed as an exhibit to the registration statement of which this prospectus is a part.

Administration. The 2014 Incentive Plan is administered by our compensation committee. Our compensation committee has the authority to, among other things, interpret the 2014 Incentive Plan, determine eligibility for, grant and determine the terms of awards under the 2014 Incentive Plan, and do all things necessary or appropriate to carry out the purposes of the 2014 Incentive Plan. Our compensation committee s determinations under the 2014 Incentive Plan are conclusive and binding.

Eligibility. Our key employees, directors, consultants and advisors are eligible to participate in the 2014 Incentive Plan.

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Authorized Shares. Subject to adjustment, as described below, the maximum number of shares of our common stock that may be delivered in satisfaction of awards under the 2014 Incentive Plan will initially be 1,785,000 shares, plus 195,890 shares that are available for grant under the 2008 Equity Incentive Plan as of the date of the adoption of the Plan. The number of shares of our common stock available for issuance under the 2014 Incentive Plan will be automatically increased annually on January 1 of each calendar year, beginning with the 2015 calendar year and ending with the 2024 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 31 (calculated by adding to the number of shares of Stock outstanding, all outstanding securities convertible into Stock on such date on an as converted basis). Our board of directors may act prior to January 1 of any year to provide that there will be no automatic increase in the number of shares available for grant under the 2014 Incentive Plan for that year (or that the increase will be less than the amount that would otherwise have automatically been made). Subject to adjustment, as described below, no more than 1,980,890 shares of our common stock may be delivered in satisfaction of incentive stock options, or ISOs, awarded under the 2014 Incentive Plan.

The shares of our common stock to be issued under the 2014 Incentive Plan may be authorized but unissued shares of our common stock or previously issued shares of our common stock acquired by us. Any shares of our common stock underlying awards that are settled in cash, or the portion of any stock option or stock appreciation right, or SAR, that expires, terminates, or is forfeited prior to the issuance of the stock thereunder, will again be available for issuance under the 2014 Incentive Plan. The number of shares of our common stock delivered in satisfaction of awards will be determined by treating as having been delivered the full number of shares of stock covered by any portion of a SAR that is settled in stock (and not only the number of shares of stock delivered in settlement), as well as by treating as having been delivered any shares withheld in payment of the exercise price of an award or in satisfaction of tax withholding requirements with respect to an award.

Section 162(m) Limits. The maximum number of shares of our common stock subject to stock options and the maximum number of shares of our common stock subject to SARs that may be granted to any participant in the 2014 Incentive Plan in any calendar year is each 875,000 shares. The maximum number of shares of our common stock subject to other awards that may be granted to any participant in the 2014 Incentive Plan in any calendar year is 293,125 shares.

Types of Awards. The 2014 Incentive Plan provides for awards of stock options, SARs, restricted stock, unrestricted stock, stock units, performance awards and other awards convertible into or otherwise based on shares of our common stock. Eligibility for stock options intended to be ISOs is limited to our employees. Dividend equivalents may also be provided in connection with an award under the 2014 Incentive Plan.

Stock options and SARs. The exercise price of a stock option, and the base price against which a SAR is to be measured, may not be less than the fair market value (or, in the case of an ISO granted to a ten percent shareholder, 110% of the fair market value) of shares of our common stock on the date of grant. Our compensation committee will determine the time or times at which stock options or SARs become exercisable and the terms on which such awards remain exercisable. Each stock option and SAR granted under the 2014 Incentive Plan will have a maximum term not to exceed ten (10) years from the date of grant (five (5) years in the case of an ISO granted to a ten percent shareholder).

Restricted and unrestricted stock. A restricted stock award is an award of shares of our common stock subject to forfeiture restrictions, while an unrestricted stock award is not subject to such restrictions.

Stock units. A stock unit award is an award denominated in shares of our common stock that entitles the participant to receive shares of our common stock or cash measured by the value of the shares of our common stock in the future. The delivery of shares of our common stock or cash under a stock unit may be subject to the satisfaction of performance conditions or other vesting conditions.

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Performance awards. A performance award is an award the vesting, settlement or exercisability of which is subject to specified performance criteria (meaning, criteria other than the mere passage of time or continuation of the participant s employment or other service relationship).

Other awards. Other awards are awards that are convertible into or otherwise based on shares of our common stock.

Performance Awards. The 2014 Incentive Plan provides for the grant of performance awards that are made based upon, and subject to achieving, performance criteria. Performance criteria with respect to those awards that are intended to qualify as performance-based compensation for purposes of Section 162(m) of the Code, or Section 162(m), to the extent applicable, are limited to an objectively determinable measure or measures of performance relating to any or any combination of the following (measured either absolutely or by reference to an index or indices and determined either on a consolidated basis or, as the context permits, on a divisional, subsidiary, line of business, project or geographical basis or in combinations thereof): sales; revenues; assets; expenses; earnings before or after deduction for all or any portion of interest, taxes, depreciation, amortization, or equity expense, whether or not on a continuing operations or an aggregate or per share basis; return on equity, investment, capital, capital employed or assets; one or more operating ratios; borrowing levels, leverage ratios or credit rating; market share; capital expenditures; cash flow; stock price; stockholder return; sales of particular products or services; customer acquisition or retention; acquisitions and divestitures (in whole or in part); joint ventures, strategic alliances, licenses or collaborations; spin-offs, split-ups and the like; reorganizations; or recapitalizations, restructurings, financings (issuance of debt or equity) or refinancings; manufacturing or process development; or achievement of clinical trial or research objectives, regulatory or other filings or approvals or other product development milestones.

To the extent consistent with the requirements for satisfying the performance-based compensation exception under Section 162(m), to the extent applicable, our compensation committee may provide in the case of any award intended to qualify for such exception that one or more of the performance criteria applicable to such award will be adjusted in an objectively determinable manner to reflect events (for example, the impact of charges for restructurings, discontinued operations, mergers, acquisitions, extraordinary items, and other unusual or non-recurring items, and the cumulative effects of tax or accounting changes, each as defined by U.S. generally accepted accounting principles) occurring during the performance period that affect the applicable performance objectives.

Vesting; Termination of Employment or Service. Our compensation committee has the authority to determine the vesting schedule applicable to each award, and to accelerate the vesting or exercisability of any award. Our compensation committee will determine the effect of termination of employment or service on an award. Unless otherwise provided by our compensation committee, upon a termination of a participant s employment or service, all unvested stock options and SARs then held by the participant will terminate and all other unvested awards will be forfeited and all vested stock options and SARs then held by the participant will remain outstanding for three months following such termination, or one year in the case of death, or, in each case, until the applicable expiration date, if earlier. All stock options and SARs held by a participant immediately prior to the participant s termination of employment or service will immediately terminate if such termination is for cause, as defined in the 2014 Incentive Plan, or occurs in circumstances that would have constituted grounds for the participant s employment or service to be terminated for cause, in the determination of the compensation committee.

Non-Transferability of Awards. Awards under the 2014 Incentive Plan may not be transferred other than by the laws of descent and distribution, unless, for awards other than ISOs, otherwise provided by our compensation committee, and then only to any transferee eligible to be covered by the provisions of Form S-8 (under the Securities Act of 1933).

Recovery of Compensation. Our compensation committee may cancel, rescind, withhold or otherwise limit or restrict any award at any time under the 2014 Incentive Plan if the participant is not in compliance with the provisions of the 2014 Incentive Plan or any award thereunder or if the participant breaches any agreement with our company with respect to non-competition, non-solicitation, confidentiality or invention assignment. Our

compensation committee also may recover any award or payments or gain in respect of any award under the 2014 Incentive Plan in accordance with any applicable company recoupment policy or as otherwise required by applicable law or applicable stock exchange listing standards.

Certain Transactions; Certain Adjustments. In the event of a consolidation, merger or similar transaction or series of related transactions, including a sale or other disposition of shares of our common stock, in which we are not the surviving corporation or that results in the acquisition of all or substantially all of our then outstanding shares of common stock by a single person or entity or by a group of persons and/or entities acting in concert, a sale of all or substantially all of our assets or our dissolution or liquidation, our compensation committee may, among other things, provide for the continuation or assumption of some or all outstanding awards, for new grants in substitution of outstanding awards, for the accelerated vesting or delivery of shares under awards or for a cash-out of outstanding awards, in each case on such terms and with such restrictions as it deems appropriate. Except as our compensation committee may otherwise determine, awards not assumed in connection with such a transaction will terminate automatically and, in the case of outstanding restricted stock, will be forfeited automatically upon the consummation of such covered transaction. In the event of a stock dividend, stock split or combination of shares, including a reverse stock split, recapitalization or other change in our capital structure that constitutes an equity restructuring within the meaning of FASB ASC 718, our compensation committee will make appropriate adjustments to the maximum number of shares of our common stock that may be delivered under, and the ISO and individual share limits included in, the 2014 Incentive Plan, and will also make appropriate adjustments to the number and kind of shares or securities subject to awards, the exercise prices of such awards or any other terms of awards affected by such change. Our compensation committee will also make the types of adjustments described above to take into account distributions and other events other than those listed above if it determines that such adjustments are appropriate to avoid distortion in the operation of the 2014 Incentive Plan.

Amendment; Termination. Our compensation committee will be able to amend the 2014 Incentive Plan or outstanding awards, or terminate the 2014 Incentive Plan as to future grants of awards, except that our compensation committee will not be able to alter the terms of an award if it would affect materially and adversely a participant s rights under the award without the participant s consent (unless expressly provided in the 2014 Incentive Plan or the right to alter the terms of an award was expressly reserved by our compensation committee at the time the award was granted). Shareholder approval will be required for any amendment to the 2014 Incentive Plan to the extent such approval is required by law, including applicable stock exchange requirements. No awards may be made under the 2014 Incentive Plan following the ten (10) year anniversary of its adoption.

Akebia Therapeutics, Inc. Cash Incentive Plan

On February 28, 2014, our board of directors adopted the Akebia Therapeutics, Inc. Cash Incentive Plan, or the Cash Incentive Plan. Following such date, annual cash award opportunities for executive officers, including our named executive officers, and other key employees will be granted under the Cash Incentive Plan. The following summary describes the material terms of the Cash Incentive Plan. This summary is not a complete description of all provisions of the Cash Incentive Plan and is qualified in its entirety by reference to the Cash Incentive Plan, which will be filed as an exhibit to the registration statement of which this prospectus is a part.

Administration. The Cash Incentive Plan will be administered by our compensation committee. Our compensation committee has authority to interpret the Cash Incentive Plan and awards granted under it, to determine eligibility for awards and to do all things necessary to administer the Cash Incentive Plan. Any interpretation or decision by the compensation committee will be final and conclusive on all participants.

Participants; Individual Limit. Our executive officers and other key employees will be selected from time to time by the compensation committee to participate in the Cash Incentive Plan. The maximum payment to any participant under the Cash Incentive Plan in any fiscal year will in no event exceed $2,000,000.

Awards. With respect to each award granted under the Cash Incentive Plan, the compensation committee will establish the performance criteria applicable to the award, the amount or amounts payable if the performance

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criteria are achieved, and such other terms and conditions as the compensation committee deems appropriate. The Cash Incentive Plan permits the grant of awards that are intended to qualify as exempt performance-based compensation under Section 162(m) of the Code, to the extent applicable, as well as awards that are not intended to so qualify. Any awards that are intended to qualify as performance-based compensation will be administered in accordance with the requirements of Section 162(m), to the extent applicable. Awards under the Cash Incentive Plan will not be required to comply with the provisions of the plan applicable to performance-based compensation under Section 162(m) if they are eligible for exemption from such provisions by reason of the transition relief under Section 162(m).

Performance Criteria. Awards under the Cash Incentive Plan will be made based on, and subject to achieving, performance criteria established by our compensation committee, which may be applied to a participant or participants on an individual basis, to a business unit or division, or to the company as a whole. Performance criteria for awards intended to qualify as performance-based compensation for purposes of Section 162(m), to the extent applicable, are limited to the objectively determinable measures of performance relating to any or any combination of the following (measured either absolutely or by reference to an index or indices or the performance of one or more companies and determined either on a consolidated basis or, as the context permits, on a divisional, subsidiary, line of business, project or geographical basis or in combinations thereof): sales; revenues; assets; expenses; earnings before or after deduction for all or any portion of interest, taxes, depreciation, amortization, or equity expense, whether or not on a continuing operations or an aggregate or per share basis; return on equity, investment, capital, capital employed or assets; one or more operating ratios; operating income or profit, including on an after-tax basis; net income; borrowing levels, leverage ratios or credit rating; market share; capital expenditures; cash flow; stock price; stockholder return; sales of particular products or services; customer acquisition or retention; acquisitions and divestitures (in whole or in part); joint ventures, strategic alliances, licenses or collaborations; spin-offs, split-ups and the like; reorganizations; or recapitalizations, restructurings, financings (issuance of debt or equity) or refinancings; manufacturing or process development; or achievement of clinical trial or research objectives, regulatory or other filings or approvals or other product development milestones.

To the extent consistent with the requirements for satisfying the performance-based compensation exception under Section 162(m), to the extent applicable, our compensation committee may provide in the case of any award intended to qualify for such exception that one or more of the performance criteria applicable to such award will be adjusted in an objectively determinable manner to reflect events (for example, the impact of charges for restructurings, discontinued operations, mergers, acquisitions, extraordinary items, and other unusual or non-recurring items, and the cumulative effects of tax or accounting changes, each as defined by U.S. generally accepted accounting principles) occurring during the performance period that affect the applicable performance objectives.

Payment under an Award. A participant will be entitled to payment under an award only if all conditions to payment have been satisfied in accordance with the Cash Incentive Plan and the terms of the award. Our compensation committee will determine the payment date or dates for awards under the Cash Incentive Plan. Following the close of the performance period, our compensation committee will determine (and, to the extent required by Section 162(m), certify) whether and to what extent the applicable performance criteria have been satisfied. Our compensation committee will then determine the actual payment, if any, under each award. Our compensation committee has the sole and absolute discretion to reduce the actual payment to be made under any award. Our compensation committee may permit a participant to defer payment of an award subject to the requirements of applicable law.

Recovery of Compensation. Awards under the Cash Incentive Plan will be subject to forfeiture, termination and rescission, and a participant who receives a payment pursuant to the Cash Incentive Plan will be obligated to return such payment to us, to the extent provided by our compensation committee in connection with a breach by the participant of the terms of the Cash Incentive Plan, an award agreement under the Cash Incentive Plan or any non-competition, non-solicitation, confidentiality or similar covenant or agreement with our company or an

overpayment of incentive compensation due to inaccurate financial data; in accordance with any applicable company recoupment policy; or as otherwise required by law or applicable stock exchange listing standards.

Amendment; Termination. Our compensation committee may amend the Cash Incentive Plan at any time, provided that any amendment will be approved by our shareholders if required by Section 162(m). Our compensation committee may terminate the Cash Incentive Plan at any time.

2014 Employee Stock Purchase Plan

In connection with this offering, on February 28, 2014, our board of directors has adopted the Akebia Therapeutics, Inc. 2014 Employee Stock Purchase Plan, or the ESPP, subject to and effective upon approval by our shareholders. The ESPP is intended to enable our eligible employees to use payroll deductions to purchase shares of our common stock and thereby acquire an interest in the future of our company. The ESPP is also intended to qualify as an employee stock purchase plan under Section 423 of the Code, or Section 423. The following summary describes the material terms of the ESPP. This summary of the ESPP is not a complete description of all provisions of the ESPP and is qualified in its entirety by reference to the ESPP, which is filed as an exhibit to the registration statement of which this prospectus is a part. As of the date of this prospectus, the initial option period under the ESPP has not commenced and our board of directors has not determined the date on which such initial option period will commence.

Administration. The ESPP is administered by our compensation committee, which has the authority to interpret the ESPP, determine eligibility under the ESPP, prescribe forms, rules and procedures relating to the ESPP and otherwise do all things necessary or appropriate to carry out the purposes of the ESPP. Our compensation committee s determinations under the ESPP are final and binding on all participants.

Eligibility. Generally, each of our employees (including employees of participating subsidiaries) will be eligible to participate in the ESPP if such employee has been continuously employed by us (or a participating subsidiary) for at least twenty (20) days as of the first day of an option period, customarily works twenty (20) hours or more per week, customarily works for more than five (5) months in any calendar year and satisfies the other requirements set forth in the ESPP. However, an employee may not be granted an option to purchase shares of our common stock under the ESPP if, immediately after the option is granted, the employee would own stock possessing 5% or more of the total combined voting power or value of all classes of our stock.

Authorized Shares. Subject to adjustment, as described below, the maximum aggregate number of shares of our common stock available for purchase pursuant to the exercise of options granted under the ESPP will be the lesser of (a) 262,500 shares, increased on each anniversary of the adoption of the ESPP by one percent (1%) of the total shares of our common stock then outstanding and (b) 739,611 shares (which is equal to five percent (5%) of the total shares of our common stock outstanding on the date of adoption of the ESPP on a fully diluted, as converted basis).

Option Periods. Unless otherwise determined by the Administrator, the ESPP provides for six-month option periods commencing on the first trading days of January and July and ending on the last trading days of June and December, respectively, of each year. The last day of each such Option Period will be an exercise date. The Administrator may change the exercise date (including the number of exercise dates within each option period) and the commencement date, ending date and duration of the option periods to the extent permitted by applicable law, provided that no exercise date will be later than 7 business days after the end of the applicable option period.

Option Grant. Subject to the limitations in the ESPP, participants in the ESPP will be granted an option on the first day of an option period to purchase shares of our common stock on the last day of the option period (i.e., the exercise date). No employee will be granted an option to purchase shares of our common stock under the ESPP if, immediately after the option is granted, he or she would hold rights to purchase shares of our common stock under all our employee stock purchase plans, including the ESPP, that accrue at a rate that exceeds $25,000 in fair market value for each calendar year.

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Participation. Eligible employees may participate in the ESPP by executing and delivering to our compensation committee a payroll deduction and participation authorization form in accordance with the rules set forth in the ESPP. Eligible employees may only participate in one option period at a time. A participant may decrease his or her payroll deduction once during an option period. Participants may end their participation in a current option period upon notice to our compensation committee and the accrued payroll deductions will be returned to the participant, without interest. Participation ends automatically upon termination of employment with us.

Purchase Price. The purchase price of a share of our common stock issued pursuant to the exercise of an option under the ESPP will be equal to 85% of the lower of the fair market value of our common stock on the first day of the option period or the exercise date.

Exercise of Option. The ESPP will permit participants to purchase shares of our common stock through payroll deductions in whole percentage amounts of up to 15% of their base pay or salary per payroll period. A participant may purchase a maximum of 1,500 shares of our common stock on any exercise date. Subject to the limitations described herein and set forth in the ESPP, on the exercise date of each option period, each participant will be deemed to have exercised his or her option and the participant s accumulated payroll deductions will be applied to purchase shares of our common stock.

Non-transferable. A participant may not transfer an option granted under the ESPP.

Change in capitalization. In the event of a change in our outstanding shares of common stock due to a stock dividend, split-up, recapitalization, merger, consolidation, reorganization, or other capital change, the aggregate number and type of shares of our common stock available under the ESPP, the number and type of shares granted under any outstanding option, and the purchase price per share under any outstanding option will be appropriately adjusted in a manner that complies with Section 423.

Merger, sale of assets. In the event of a sale of all or substantially all of our assets, or a merger or similar transaction in which the company is not the surviving corporation or that results in the acquisition of the company by another person, the compensation committee may, in its discretion, (a) if the company is merged with or acquired by another corporation, provide that each outstanding option will be assumed or exchanged for a substitute option granted by the acquiror or successor corporation, (b) cancel each outstanding option, and/or (c) terminate the option period then in effect.

Amendment; Termination. The board has the right to amend, suspend or terminate the ESPP at any time. Unless terminated earlier, the ESPP will automatically terminate in 2024.

Director Compensation

The following table sets forth a summary of the compensation we paid to our non-employee directors during 2013. Other than as set forth in the table below, we did not pay any compensation, make any equity awards or non-equity awards to, or pay any other compensation to any of the other non-employee members of our board of directors in 2013 and 2012. Mr. Butler, our President and Chief Executive Officer, and Dr. Gardner, our former President and Chief Executive Officer, received no compensation for their service as a director, and, consequently, are not included in this table. The compensation received by Mr. Butler and Dr. Gardner as employees during 2013 and 2012 is presented in Summary Compensation Table above.

	2013		2012	
Name	Stock Awards ($)[1]	All Other Compensation ($)[2]	Stock Awards ($)	All Other Compensation ($)[2]
Anupam Dalal, M.D.		6,398		5,238
Campbell Murray, M.D.				
John Rice		739		863
Paul Weiss		927		6,000
Jack Nielsen		9,236		
Giovanni Ferrara		209		
Duane Nash	352,769[3]			

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(1) The amount reported in the Stock Awards column represents the retrospective fair value of the stock awards as of the grant date.
(2) Amounts represent reimbursement of travel and expenses in connection with the individual s service as a director.
(3) Amount reflects 47,525 shares of restricted stock. Under the terms of the December 23, 2013 restricted stock agreement, 50% of the unvested shares vest on December 23, 2014 and the remaining 50% vests quarterly over the following three years; provided that no shares or restricted stock would vest prior to the occurrence of a liquidity event. Vesting of all restricted shares shall accelerate in connection with an acquisition event pursuant to the terms of the restricted stock agreement. As of December 31, 2013, none of our directors other than the Dr. Nash held stock options or unvested stock awards, and Dr. Nash held 47,525 shares of restricted stock and no stock option.

Non-Employee Director Compensation Policy

Our board of directors has adopted a non-employee director compensation policy, effective as of the completion of this offering, that is designed to enable us to attract and retain, on a long-term basis, highly qualified non-employee directors. Under the policy, each individual who is not an employee (a non-employee director) will be paid cash compensation from and after the completion of this offering, as set forth below:

	Annual Retainer
Board of Directors:	
All non-employee members	$ 35,000
Additional retainer for chair*	$ 20,000
Audit Committee:	
Members	$ 7,500
Additional retainer for chair	$ 15,000
Compensation Committee:	
Members	$ 5,000
Additional retainer for chair	$ 10,000
Nominating and Corporate Governance Committee:	
Members	$ 7,500
Additional retainer for chair	$ 3,750

* In the event a non-employee director is one of two concurrently serving chairmen of our board of directors, the annual additional retainer for each co-chair will be $10,000.

Under our non-employee director compensation policy, each non-employee director who is initially appointed or elected to our board of directors will be eligible to receive a grant of stock option to purchase 10,000 shares of our common stock under our 2014 Incentive Plan at the time of his or her initial appointment or election to our board of directors, which will vest as to 25% of the stock option on the one-year anniversary of the date of grant and the remaining 75% of the stock option will vest ratably on the first day of each calendar quarter between the one-year anniversary of the date of grant and the fourth anniversary of the date of grant, subject to the non-employee director s continuous service through the applicable vesting date. In addition, each continuing non-employee director who has served on the board of directors for at least six months as of the date of any annual meeting will be eligible to receive, on the date of such annual meeting, a grant of stock options to purchase 5,000 shares of our common stock under our 2014 Incentive Plan, which will vest on the first anniversary of the grant date (or, if earlier, immediately prior to the next annual meeting following the date of grant), subject to the non-employee director s continuous service through the applicable vesting date. These stock options will be granted with an exercise price equal to the fair market value of a share of our common stock on the date of grant and will have a 10-year term. Our board of directors has adopted a form of stock option award under the 2014 Incentive Plan (as described below) for our non-employee directors, under which initial and subsequent stock option grants will vest in full upon a change in control (as defined in the form of stock option agreement).

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Certain Relationships and Related Party Transactions

Since January 1, 2010, we have engaged in the following transactions with our directors and executive officers and holders of more than 5% of our voting securities and affiliates of our directors, executive officers and such 5% stockholders. We believe that all of the transactions described below were made on terms no less favorable to us than could have been obtained from unaffiliated third parties.

Preferred Stock Financings

Series A Preferred Stock Financing

In June 2010, we issued and sold an aggregate of 125,000 shares of our Series A preferred stock at a purchase price of $40.00 per share for an aggregate purchase price of $5 million. The following table sets forth the number of shares of our Series A preferred stock that we issued to our directors, executive officers and 5% stockholders at the time of such issuance and their affiliates, in connection with this transaction and the aggregate cash purchase price paid by these related parties:

Investor	Shares of Series A Preferred Stock	Purchase Price ($)
Triathlon Medical Ventures	12,453	498,120
Novartis Bioventures Ltd.	61,250	2,450,000
Venture Investors Early Stage Fund IV	32,747	1,309,889
Kearny Venture Partners, L.P. and affiliates[1]	6,806	272,226
Joseph Gardner[2]	2,834	113,345
Ian Howes[3]	1,250	50,000

(1) Consists of 3,335 shares purchased by Kearny Venture Partners, L.P., 68 shares purchased by Kearny Venture Partners Entrepreneurs Fund, L.P., and 3,403 shares purchased by Thomas Weisel Healthcare Venture.

(2) Consists of 625 shares purchased by Joseph Gardner and 2,209 shares purchased by the Gardner Family Trust. Dr. Gardner was our former President and Chief Executive Officer.

(3) Consists of 1,250 shares purchased by Ian A.W. Howes, IRA, Sterling Trust Custodian. Mr. Howes was our former Chief Financial Officer.

Series B Preferred Stock Financing

In April 2011 and December 2011, we issued and sold an aggregate of 1,287,525 shares of our Series B preferred stock at a purchase price of $14.00 per share for an aggregate purchase price of $18,025,341. As part of this financing, various trusts and other entities affiliated with Muneer A. Satter collectively purchased 260,873 shares of our Series B preferred stock and immediately following this purchase became a beneficial owner of more than 5% of our voting securities. Furthermore, as part of this financing, AgeChem Venture Fund L.P. purchased 173,915 shares of our Series B preferred stock and immediately following this purchase became a beneficial owner of more than 5% of our voting securities.

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The following table sets forth the number of shares of our Series B preferred stock that we issued to our directors, executive officers and 5% stockholders at the time of such issuance and their affiliates, in connection with this transaction and the aggregate cash purchase price paid by these related parties:

Investor	Shares of Series B Preferred Stock	Purchase Price ($)
Triathlon Medical Ventures	124,502	1,743,024
Novartis Bioventures Ltd.	347,831	4,869,630
Venture Investors Early Stage Fund IV	173,915	2,434,815
Kearny Venture Partners, L.P. and affiliates(1)	88,478	1,238,692
Joseph Gardner(2)	18,882	264,354
Robert Shalwitz	2,070	28,986
Ian Howes(3)	5,797	81,161

(1) Consists of 43,355 shares purchased by Kearny Venture Partners, L.P., 884 shares purchased by Kearny Venture Partners Entrepreneurs Fund, L.P., and 44,239 shares purchased by Thomas Weisel Healthcare Venture.
(2) Consists of 11,594 shares purchased by Joseph Gardner and 7,288 shares purchased by the Gardner Family Trust.
(3) Consists of 5,797 shares purchased by Ian A.W. Howes, IRA, Sterling Trust Custodian.

Series X Preferred Stock Financing

In July 2012 and March 2013, we issued and sold an aggregate of 50,000 shares of our Series X preferred stock, at a purchase price of $100.00 per share, for an aggregate purchase price of $5,000,002.

The following table sets forth the number of shares of our Series X preferred stock that we issued to our directors, executive officers and 5% stockholders at the time of such issuance and their affiliates, in connection with this transaction and the aggregate cash purchase price paid by these related parties:

Investor	Shares of Series X Preferred Stock	Purchase Price ($)
Triathlon Medical Ventures	6,576	657,576
Novartis Bioventures Ltd.	15,211	1,521,064
Venture Investors Early Stage Fund IV	8,253	825,348
Kearny Venture Partners, L.P. and affiliates(1)	4,490	449,004
Trusts and Other Entities Affiliated with Muneer A. Satter	3,504	350,394
Joseph Gardner(2)	2,042	204,165
Ian Howes(3)	406	40,631
AgeChem Venture Fund L.P.	2,240	224,026

(1) Consists of 220 shares purchased by Kearny Venture Partners, L.P., 45 shares purchased by Kearny Venture Partners Entrepreneurs Fund, L.P., and 2,245 shares purchased by Thomas Weisel Healthcare Venture.
(2) Consists of 1,694 shares purchased by Joseph Gardner and 348 shares purchased by the Gardner Family Trust.
(3) Consists of 406 shares purchased by Ian A.W. Howes, IRA, Sterling Trust Custodian.

Series C Preferred Stock Conversion

In May 2013, we issued an aggregate of 357,143 shares of Series C preferred stock at an exchange rate of 7.14286 shares of Series C preferred stock for every share of Series X preferred stock.

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The following table sets forth the number of shares of our Series C preferred stock that we issued to our directors, executive officers and 5% stockholders at the time of such issuance and their affiliates, in exchange for their shares of Series X preferred stock:

Investor	Shares of Series C Preferred Stock
Triathlon Medical Ventures	6,576
Novartis Bioventures Ltd.	15,211
Venture Investors Early Stage Fund IV	8,253
Kearny Venture Partners, L.P. and affiliates[1]	4,490
Trusts and Other Entities Affiliated with Muneer A. Satter	3,504
Joseph Gardner[2]	2,042
Ian Howes[3]	406
AgeChem Venture Fund L.P.	2,240

(1) Consists of 2,200 shares held by Kearny Venture Partners, L.P., 45 shares held by Kearny Venture Partners Entrepreneurs Fund, L.P., and 2,245 shares held by Thomas Weisel Healthcare Venture.
(2) Consists of 1,694 shares held by Joseph Gardner and 348 shares held by the Gardner Family Trust.
(3) Consists of 406 shares held by Ian A.W. Howes, IRA, Sterling Trust Custodian.

Series C Preferred Stock Financing

In May 2013, we issued and sold an aggregate of 2,945,742 shares of our Series C preferred stock, at a purchase price of $14.00 per share, for an aggregate purchase price of $41,240,388. As part of this financing, Novo A/S purchased 714,285 shares of our Series C preferred stock and immediately following this purchase became a beneficial owner of more than 5% of our voting securities.

The following table sets forth the number of shares of our Series C preferred stock that we issued to our directors, executive officers and 5% stockholders at the time of such issuance and their affiliates, in connection with this transaction and the aggregate cash purchase price paid by these related parties:

Investor	Shares of Series C Preferred Stock	Purchase Price ($)
Triathlon Medical Ventures	71,428	999,992
Novartis Bioventures Ltd.	600,000	8,400,000
Venture Investors Early Stage Fund IV	142,858	2,000,012
Kearny Venture Partners, L.P. and affiliates[1]	357,143	5,000,002
Trusts and Other Entities Affiliated with Muneer A. Satter	471,425	6,599,950
Robert Shalwitz	2,500	35,000
Joseph Gardner	14,285	199,990
Ian Howes	7,142	99,988

(1) Consists of 292,733 shares purchased by Kearny Venture Partners, L.P., 5,970 shares purchased by Kearny Venture Partners Entrepreneurs Fund, L.P., and 58,440 shares purchased by Thomas Weisel Healthcare Venture.

Indemnification Agreements

Prior to the completion of this offering, we expect to enter into indemnification agreements with each of our directors and executive officers. These agreements will require us to indemnify these individuals and, in certain cases, affiliates of such individuals, to the fullest extent permissible under Delaware law against liabilities that may arise by reason of their service to us or at our direction, and to advance expenses incurred as a result of any proceeding against them as to which they could be indemnified.

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Employment Agreements

See the Executive Compensation Employment Agreements with Our Named Executive Officers section of this prospectus for a further discussion of these agreements.

Investors Rights Agreement

In connection with our Series C preferred stock financing, on May 10, 2013, we entered into the Third Amended and Restated Investors Rights Agreement, or the investors rights agreement, with the holders of all of our then-outstanding shares of preferred stock including certain of our executive officers and entities with which certain of our directors are affiliated. The agreement provides that these holders have the right to demand that we file a registration statement with respect to the common stock issued upon conversion of the preferred stock. These holders may also request that shares of common stock held by them be included in certain registration statements that we are otherwise filing. In connection with this offering, we entered into the Fourth Amended and Restated Investors Rights Agreement with the holders of all our outstanding shares of preferred stock including certain of our executive officers and entities with which certain of our directors are affiliated. The Fourth Amended and Restated Investors Rights agreement contains substantially the same terms as the investors rights agreement. See Description of Capital Stock Registration Rights.

Right of First Refusal and Co-Sale Agreement

In connection with our Series C preferred stock financing, on May 10, 2013, we entered into an amendment to the Second Amended and Restated Right of First Refusal and Co-Sale Agreement with the holders of all of our then-outstanding shares of preferred stock including certain of our executive officers and entities with which certain of our directors are affiliated. Pursuant to the terms of this agreement, in the event of a proposed sale of shares of our common or preferred stock, the seller is required to first offer such shares to the company and to the other investors, subject to certain conditions and restrictions. This agreement will terminate upon the completion of this offering.

Voting Agreement

In connection with our Series C preferred stock financing on May 10, 2013, we entered into the Third Amended and Restated Voting Agreement with the holders of all of our then-outstanding shares of preferred stock including certain of our executive officers and entities with which certain of our directors are affiliated, with respect to the election of directors and certain other matters. All of our current directors were elected pursuant to the terms of this agreement. This agreement will terminate upon the completion of this offering.

Services Agreement

In connection with the spin out of our programs focused on the treatment of diabetic eye disease and inflammatory bowel disease into Aerpio, we entered into two administrative services agreements with Aerpio, the first on December 22, 2011, as amended and restated on August 27, 2012, and the second on November 1, 2012.

Under the terms of the administrative services agreements, starting in 2012, we and Aerpio have obtained from and provided to each other certain services. These services include consulting services, access to Aerpio s office facilities in Ohio and Michigan, shared use of IT equipment (including internet and phone networks), and use of Aerpio s office equipment and furniture. The consulting services include research and development, finance, and administrative services. The agreement also requires the parties to cooperate with each other to facilitate the transition of certain assets, employees and programs to Aerpio in connection with the spin out, and for us to make certain of our employees, including Dr. Shalwitz, our Chief Medical Officer, available for specified amounts of time to work on Aerpio projects.

The scope of consulting services provided to Aerpio under the agreement has declined since 2012, and we anticipate this trend to continue. Aerpio reimbursed us for employee costs in the amount of $2.0 million for the year ended December 31, 2012 and $1.0 million for the year ended December 31, 2013. Aerpio paid us for facility related charges in the amount of $0.2 million for the year ended December 31, 2012 and $0.3 million

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for the year ended December 31, 2013. We paid Aerpio $0.2 million for the year ended December 31, 2012, and $0.3 million for the year ended December 31, 2013. As of December 31, 2013, the amounts due from Aerpio to us total $135,339, and the amounts due from us to Aerpio total $62,735.

Promissory Notes

We issued promissory notes to Joseph Gardner, our former President and Chief Executive Officer, in the aggregate amount of $140,839. Dr. Gardner used these promissory notes to purchase restricted stock awards, as described in Executive Compensation 2012 Outstanding Equity Awards at Fiscal Year-End. The promissory notes were amended in 2013 to forgive a portion of the principal owed and to reduce the interest rate from 6% to 3% per annum. As of February 13, 2013, the current balance of the outstanding promissory notes was $112,831. The promissory notes are repayable at the earlier of (a) an initial public offering; (b) the sale of the company or substantially all of its assets; (c) the termination of the employee; or (d) five years from origination.

Related Person Transactions Policy

We have adopted a related person transaction approval policy that will govern the review of related person transactions following the closing of this offering. Pursuant to this policy, if we want to enter into a transaction with a related person or an affiliate of a related person, our Chief Financial Officer will review the proposed transaction to determine, based on applicable NASDAQ and SEC rules, if such transaction requires pre-approval by the audit committee and/or board of directors. If pre-approval is required, such matters will be reviewed at the next regular or special audit committee and/or board of directors meeting. We may not enter into a related person transaction unless our Chief Financial Officer has either specifically confirmed in writing that no further reviews are necessary or that all requisite corporate reviews have been obtained.

Participation in this Offering

Certain of our existing stockholders and their affiliated entities, including holders of more than 5% of our common stock, have agreed to purchase an aggregate of 887,929 shares of our common stock in this offering at the initial public offering price.

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Principal Stockholders

The following table sets forth information relating to the beneficial ownership of our common stock as of February 28, 2014 by: each person, or group of affiliated persons, known by us to beneficially own more than 5% of our outstanding shares of common stock; each of our directors; each of our named executive officers; and all directors and executive officers as a group.

The number of shares beneficially owned by each entity, person, director or executive officer is determined in accordance with the rules of the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. Under such rules, beneficial ownership includes any shares over which the individual has sole or shared voting power or investment power as well as any shares that the individual has the right to acquire within 60 days of February 28, 2014 through the exercise of any stock options or other rights. Except as otherwise indicated, and subject to applicable community property laws, the persons named in the table have sole voting and investment power with respect to all shares of common stock held by that person.

The percentage of shares beneficially owned is computed on the basis of 13,462,580 shares of our common stock outstanding as of February 28, 2014, which reflects the assumed conversion of all of our outstanding shares of preferred stock into an aggregate of 12,077,070 shares of common stock as of such date. Shares of our common stock that a person has the right to acquire within 60 days of February 28, 2014 are deemed outstanding for purposes of computing the percentage ownership of the person holding such rights, but are not deemed outstanding for purposes of computing the percentage ownership of any other person, except with respect to the percentage ownership of all directors and executive officers as a group. Unless otherwise indicated below, the address for each beneficial owner listed is c/o Akebia Therapeutics, Inc., 245 First Street, Suite 1100 Cambridge, MA 02142.

Certain of our existing stockholders and their affiliated entities, including holders of more than 5% of our common stock, have agreed to purchase shares of our common stock in this offering at the initial public offering price. The following table does not reflect any such purchases by these existing principal stockholders or their affiliated entities.

Name and address of beneficial owner	Number of shares beneficially owned**	Percentage of shares beneficially owned	
		Before offering	After offering
5% or greater stockholders:			
Novartis Bioventures Ltd.[2]	3,214,972	23.9%	16.6%
Venture Investors Early Stage Fund IV[3]	1,447,755	11.0%	7.5%
Trusts and Other Entities Affiliated with Muneer A. Satter[6]	1,435,184	10.7%	7.4%
Kearny Venture Partners, L.P. and related funds[4]	1,335,594	9.9%	6.9%
Novo A/S[5]	1,325,636	9.9%	6.9%
Triathlon Medical Ventures[1]	1,114,080	8.3%	5.8%
Directors and named executive officers:			
Joseph H. Gardner[7]	488,918	3.6%	2.5%
John P. Butler[10]	0	*	*
William Daly[8]	133,728	1.0%	*
Robert Shalwitz, M.D.[9]	370,533	2.7%	1.9%
Muneer A. Satter[6]	1,435,184	10.7%	7.4%
Campbell Murray, M.D.[2]	3,214,972	23.9%	16.6%
Jack Nielsen	0	*	*
Anupam Dalal, M.D.	0	*	*
Giovanni Ferrara[2]	3,214,972	23.9%	16.6%

Kim Dueholm	0	*	*
Duane Nash	47,524	*	*
Michael S. Wyzga[11]	0	*	*
All executive officers and directors as a group (12 persons)	5,140,836	37.9%	26.5%

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* Represents beneficial ownership of less than one percent of our outstanding common stock.

** Fractional shares have been rounded down to the nearest whole number.

(1) Consists of 35,000 shares of common stock, 640,477 shares of common stock issuable upon conversion of Series A preferred stock, 217,878 shares of common stock issuable upon conversion of Series B preferred stock and 220,725 shares of common stock issuable upon conversion of Series C preferred stock held by Triathlon Medical Ventures Fund. Its general partner, Triathlon Medical Ventures LLC, has sole voting and investment control over the shares owned by Triathlon Medical Ventures Fund. The members of Triathlon Medical Ventures LLC, John Rice, Carrie Bates, Suzette Dutch and Dennis Costello, have sole voting and investment power for Triathlon Medical Ventures LLC with respect to its voting power in its capacity as the general partner for the shares held by Triathlon Medical Ventures Fund.

(2) Consists of 1,285,155 shares of common stock issuable upon conversion of Series A preferred stock, 608,703 shares issuable upon conversion of Series B preferred stock and 1,321,114 shares of common stock issuable upon conversion of Series C preferred stock held by Novartis Bioventures Ltd, a Bermuda corporation. The board of directors of Novartis Bioventures Ltd. has sole voting and investment control and power over such shares. None of the members of its board of directors has individual voting or investment power with respect to such shares and each disclaims beneficial ownership of such shares. Mr. Campbell Murray and Mr. Giovanni Ferrara, two members of our Board of Directors (of which Mr. Murray is co-Chairman), are also employees of a corporation that is affiliated with Novartis Bioventures Ltd. They also disclaim beneficial ownership of shares held by Novartis Bioventures Ltd., except to the extent of their pecuniary interest arising as a result of their employment by that affiliate. Novartis Bioventures Ltd is an indirectly-owned subsidiary of Novartis AG. Novartis Bioventures Ltd. has agreed to purchase 182,590 shares in this offering. This will increase their after offering ownership in Akebia to 17.6%.

(3) Consists of 767,172 shares of common stock issuable upon conversion of Series A preferred stock, 304,351 shares of common stock issuable upon conversion of Series B preferred stock and 376,232 shares of common stock issuable upon conversion of Series C preferred stock. Venture Investors Early Stage Fund IV Limited Partnership is a Delaware Limited Partnership. Its General Partner, VIESF IV GP LLC, has sole voting and investment control over the shares owned by Venture Investors Early Stage Fund IV Limited Partnership. The members of VIESF IV GP LLC, John Neis, Paul M. Weiss, Scott Button, George Arida, James R. Adox, Loren G. Peterson, and Venture Investors Southeast LLC (of which Roger H. Ganser is the sole member), have sole voting and investment power for VIESF IV GP LLC with respect to its voting power in its capacity as General Partner for the shares held by Venture Investors Early Stage Fund IV Limited Partnership. None of the members of VIESF IV GP LLC has individual voting or investment power with respect to such shares and each disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein. The address of Venture Investors Early Stage Fund IV Limited Partnership is 505 South Rosa Road, Suite 201, Madison, Wisconsin, 53719. Venture Investors Early Stage Fund IV has agreed to purchase 73,036 shares in this offering. This will increase their after offering ownership in Akebia to 7.9%.

(4) Consists of (i) 223,030 shares of common stock issuable upon the conversion of Series A preferred stock, 75,870 shares of common stock issuable upon conversion of Series B preferred stock and 575,032 shares of common stock issuable upon conversion of Series C preferred stock that are held directly by Kearny Venture Partners, L.P. (KVP), (ii) 4,548 shares of common stock issuable upon the conversion of Series A preferred stock, 1,547 shares of common stock issuable upon conversion of Series B preferred stock and 11,727 shares of common stock issuable upon conversion of Series C preferred stock held by Kearny Venture Partners Entrepreneurs Fund, L.P. (KVPE), and (iii) 227,579 shares of common stock issuable upon conversion of Series A preferred stock, 77,418 shares of common stock issuable upon conversion of Series B preferred stock and 138,843 shares of common stock issuable upon conversion of Series C preferred stock that are held directly by Thomas Weisel Healthcare Venture Partners, L.P. (TWHVP). Each of KVP, KVPE and TWHVP is a Delaware limited partnership. The general partner of both KVP and KVPE is Kearny Venture Associates, L.L.C. (KVA). KVA has the sole voting and investment control over the shares owned by KVP and KVPE, and the Managing Members of KVA share in the voting and investment control over such shares controlled by KVA. The Managing Members of KVA are Caley Castelein, Richard Spalding and James Shapiro. None of the Managing Members of KVA has individual voting or investment power with respect to such shares and each disclaims beneficial ownership of such shares

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except to the extent of any pecuniary interest therein. The address of KVA is 88 Kearny Street, San Francisco, CA 94108. The general partner of TWHVP is Thomas Weisel Healthcare Venture Partners LLC (TWP GP). TWP GP has the sole voting and investment control over the shares owned by TWHVP, and the investment committee of TWP GP has sole voting and investment control over the shares controlled by TWP GP. The investment committee of TWP GP consists of Richard Spalding and James Shapiro, neither of whom has individual voting or investment power with respect to such shares and each disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein. The address of TWP GP is One Montgomery St., San Francisco, CA 94104. KVP has agreed to purchase 216,057 shares in this offering and KVPE has agreed to purchase 4,409 shares. This will increase the after offering ownership of Kearny Venture Partners, L.P. and their related funds in Akebia to 8.1%.

(5) Consists of 1,325,636 shares of common stock issuable upon conversion of Series C preferred stock. Novo A/S is a Danish limited liability company. The board of directors of Novo A/S, which consists of Sten Scheibye, Göran Ando, Jørgen Boe, Jeppe Christiansen, Steen Risgaard and Per Wold Olsen, has shared investment and voting control with respect to the shares held by Novo A/S and may exercise such control only with the support of a majority of the members of the Novo A/S board of directors. As such, no individual member of the Novo A/S board of directors is deemed to hold any beneficial ownership or reportable pecuniary interest in the shares held by Novo A/S. Mr. Nielsen and Mr. Dueholm, two members of our board of directors, are employed as Partners of Novo A/S. Neither Mr. Nielsen nor Dr. Dueholm are deemed beneficial owners of, nor do they have a reportable pecuniary interest in, the shares held by Novo A/S. The address of Novo A/S is Tuborg Havnevej 19, 2900 Hellerup, Denmark. Novo A/S has agreed to purchase 182,590 shares in this offering. This will increase their after offering ownership in Akebia to 7.9%.

(6) Consists of 456,526 shares of common stock issuable upon conversion of Series B preferred stock and 978,658 shares of common stock issuable upon conversion of Series C preferred stock held by Muneer A. Satter Revocable Trust and various other trusts and other entities for which Mr. Satter serves as trustee, investment advisor or manager and, in such capacity, has sole voting and dispositive control over all such shares. Various trusts and other entities for which Mr. Satter serves as trustee, investment advisor or manager and, in such capacity, has sole voting and dispositive control over all such shares have agreed to purchase a combined total of 91,295 shares in this offering. This will increase their collective ownership in Akebia to 7.8%.

(7) Joseph Gardner is the Company s former Chief Executive Officer. This number consists of (i) 216,717 shares of common stock, 105,637 shares of restricted stock, 45,194 shares of common stock issuable upon conversion of Series A preferred stock, 20,290 shares of common stock issuable upon conversion of Series B preferred stock and 49,185 shares of common stock issuable upon conversion of Series C preferred stock held by Joseph Gardner and (ii) 34,509 shares of common stock issuable upon conversion of Series A preferred stock, 12,754 shares of common stock issuable upon conversion of Series B preferred stock and 4,632 shares of common stock issuable upon conversion of Series C preferred stock held by the Gardner Family Trust.

(8) Consists of 108,592 shares of restricted stock and 25,146 shares of common stock issuable upon conversion of Series C preferred stock.

(9) Consists of (i) 20,000 shares of common stock, 214,980 shares of restricted stock, 4,247 shares of common stock issuable upon conversion of Series A preferred stock, 3,623 shares of common stock issuable upon conversion of Series B preferred stock and 4,660 shares of common stock issuable upon conversion of Series C preferred stock held by Robert Shalwitz and (ii) 17,015 shares of common stock issuable upon conversion of Series A preferred stock held by Fred Shalwitz Trust.

(10) John Butler, the Company s President and Chief Executive Officer, agreed to purchase 13,850 shares in this offering. This will not change his ownership percentage.

(11) Michael S. Wyzga agreed to purchase 1,500 shares in this offering. This will not change his ownership percentage.

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Description of Capital Stock

General

The following description of our capital stock is intended as a summary only and is qualified in its entirety by reference to our ninth amended and restated certificate of incorporation and amended and restated bylaws that will be in effect at the closing of this offering, which will be filed as exhibits to the registration statement of which this prospectus is a part, and to the applicable provisions of the Delaware General Corporation Law. We refer in this section to our ninth amended and restated certificate of incorporation as our certificate of incorporation, and we refer to our amended and restated bylaws as our bylaws. The description of our capital stock reflects changes to our capital structure that will occur upon the closing of this offering.

Upon the closing of this offering, our authorized capital stock will consist of 175,000,000 shares of our common stock, par value $0.00001 per share, and 25,000,000 shares of our preferred stock, par value $0.00001 per share, all of which preferred stock will be undesignated.

As of December 31, 2013, we had issued and outstanding:

- 1,383,345 shares of our common stock, which included 957,189 shares of restricted stock;
- 5,324,948 shares of our preferred stock that were convertible into 12,002,329 shares of our common stock as of such date; and
- options to purchase a total of 1,251,398 shares of our common stock with a weighted-average exercise price of $1.01 per share.

As of December 31, 2013, we had 44 stockholders of record.

Common Stock

Dividend Rights. Subject to preferences that may apply to shares of preferred stock outstanding at the time, holders of outstanding shares of common stock will be entitled to receive dividends out of assets legally available at the times and in the amounts as the board of directors may from time to time determine.

Voting Rights. Each outstanding share of common stock will be entitled to one vote on all matters submitted to a vote of stockholders. Holders of shares of our common stock shall have no cumulative voting rights.

Conversion or Redemption Rights. Our common stock will be neither convertible nor redeemable.

Liquidation Rights. Upon our liquidation, dissolution or winding up, the holders of our common stock will be entitled to receive pro rata our assets which are legally available for distribution, after payment of all debts and other liabilities and the satisfaction of any liquidation preference granted to the holders of any then-outstanding shares of preferred stock.

Rights and Preferences. Holders of common stock have no preemptive, conversion or subscription rights and there are no redemption or sinking fund provisions applicable to the common stock. The rights, preferences and privileges of the holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate in the future.

Preferred Stock

All currently outstanding shares of preferred stock will be converted automatically to common stock upon the completion of this offering.

Following the completion of this offering, our board of directors will have the authority, without further action by our stockholders, to issue up to 25,000,000 shares of preferred stock in one or more series, to establish from

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time to time the number of shares to be included in each such series, to fix the rights, preferences and privileges of the shares of each wholly unissued series and any qualifications, limitations or restrictions thereon, and to increase or decrease the number of shares of any such series, but not below the number of shares of such series then outstanding.

Our board of directors may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of our common stock. The purpose of authorizing our board of directors to issue preferred stock and determine its rights and preferences is to eliminate delays associated with a stockholder vote on specific issuances. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions and other corporate purposes, could, among other things, have the effect of delaying, deferring or preventing a change in control of us and may adversely affect the market price of our common stock and the voting and other rights of the holders of our common stock. It is not possible to state the actual effect of the issuance of any shares of preferred stock on the rights of holders of common stock until the board of directors determines the specific rights attached to that preferred stock.

We have no present plans to issue any shares of preferred stock.

Registration Rights

After our initial public offering, holders of 13,171,517 shares of our common stock issued or issuable will be entitled to certain rights with respect to registration of such shares under the Securities Act. These shares are collectively referred to herein as registrable shares. These rights are provided under the terms of the investors rights agreement, and include demand registration rights, Form S-3 registration rights and piggyback registration rights. These registration rights are subject to conditions and limitations, including the right, in certain circumstances, of the underwriters of an offering to limit the number of shares included in such registration and our right, in certain circumstances, not to effect a requested S-1 or S-3 registration within 60 days before or 180 days following our estimated date of filing of a registration statement pertaining to an underwritten public offering of securities for the account of an offering of our securities, including this offering.

Demand Registration Rights

Under the terms of the investors rights agreement, following the six-month anniversary of the completion of this offering, the holders of at least 30% of the registrable shares may require us to file a registration statement on Form S-1 under the Securities Act at our expense with respect to the resale of their registrable shares as soon as practicable, and in any event within 60 days after the date of the request for registration. We are required to effect only two registrations pursuant to this provision of the investors rights agreement.

Under the terms of the investors rights agreement, if we are eligible to file a registration statement on Form S-3, the holders of at least 30% of the registrable shares may require us to file a registration statement on Form S-3 at our expense with respect to the resale of their registrable shares as soon as practicable, and in any event within 45 days after the date of the request for registration. We are required to effect only three registrations pursuant to this provision of the investors rights agreement.

Piggyback Registration Rights

Under the terms of the investors rights agreement, if we propose to register any of our common stock under the Securities Act in connection with the public offering of such securities solely for cash except for certain excluded registrations, the holders of registrable shares are entitled to notice of such registration and to request that we include registrable shares for resale on such registration statement, subject to our right to terminate or withdraw any registration we initiate prior to its effective date and the right of any underwriter to limit the number of shares included in such registration.

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Expenses of Registration

We will pay all expenses relating to any demand, Form S-3 or piggyback registration, other than underwriting discounts, selling commissions and stock transfer taxes applicable to the sale of registrable securities, subject to specified conditions and limitations.

Anti-Takeover Effects of Our Certificate of Incorporation and Our Bylaws

Our certificate of incorporation and bylaws will contain certain provisions that are intended to enhance the likelihood of continuity and stability in the composition of the board of directors and which may have the effect of delaying, deferring or preventing a future takeover or change in control of the company unless such takeover or change in control is approved by the board of directors.

These provisions include:

Classified Board. Our certificate of incorporation will provide that our board of directors will be divided into three classes of directors, with the classes as nearly equal in number as possible. As a result, approximately one-third of our board of directors will be elected each year. The classification of directors will have the effect of making it more difficult for stockholders to change the composition of our board. Our certificate of incorporation will also provide that, subject to any rights of holders of preferred stock to elect additional directors under specified circumstances, the number of directors will be fixed exclusively pursuant to a resolution adopted by our board of directors. Upon completion of this offering, we expect that our board of directors will have seven members.

Action by Written Consent; Special Meetings of Stockholders. Our certificate of incorporation will provide that stockholder action can be taken only at an annual or special meeting of stockholders and cannot be taken by written consent in lieu of a meeting. Our certificate of incorporation and the bylaws will also provide that, except as otherwise required by law, special meetings of the stockholders can be called only by or at the direction of the board of directors pursuant to a resolution adopted by a majority of the total number of directors. Stockholders will not be permitted to call a special meeting or to require the board of directors to call a special meeting.

Removal of Directors. Our certificate of incorporation will provide that our directors may be removed only for cause by the affirmative vote of at least 75% of the votes that all our stockholders would be entitled to cast in an annual election of directors, voting together as a single class, at a meeting of the stockholders called for that purpose. This requirement of a supermajority vote to remove directors could enable a minority of our stockholders to prevent a change in the composition of our board.

Advance Notice Procedures. Our bylaws will establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to the board of directors. Stockholders at an annual meeting will only be able to consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of the board of directors or by a stockholder who was a stockholder of record on the record date for the meeting, who is entitled to vote at the meeting and who has given our Secretary timely written notice, in proper form, of the stockholder s intention to bring that business before the meeting. Although the bylaws will not give the board of directors the power to approve or disapprove stockholder nominations of candidates or proposals regarding other business to be conducted at a special or annual meeting, the bylaws may have the effect of precluding the conduct of certain business at a meeting if the proper procedures are not followed or may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect its own slate of directors or otherwise attempting to obtain control of the company.

Super Majority Approval Requirements. The Delaware General Corporation Law generally provides that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation s

certificate of incorporation or bylaws, unless either a corporation s certificate of incorporation or bylaws requires a greater percentage. A majority vote of our board of directors or the affirmative vote of holders of at least 75% of the total votes of the outstanding shares of capital stock of the Company entitled to vote with respect thereto, voting together as a single class, will be required to amend, alter, change or repeal the bylaws. In addition, the affirmative vote of the holders of at least 75% of the total votes of the outstanding shares of capital stock of the Company entitled to vote with respect thereto, voting together as a single class, will be required to amend, alter, change or repeal, or to adopt any provisions inconsistent with, any of the provisions in our certificate of incorporation relating to amendments to our certificate of incorporation and bylaws and as described under Action by Written Consent; Special Meetings of Stockholders , Classified Board and Removal of Directors above. This requirement of a supermajority vote to approve amendments to our bylaws and certificate of incorporation could enable a minority of our stockholders to exercise veto power over any such amendments.

Authorized but Unissued Shares. Our authorized but unissued shares of common stock and preferred stock will be available for future issuance without stockholder approval. These additional shares may be utilized for a variety of corporate purposes, including future public offerings to raise additional capital and corporate acquisitions. The existence of authorized but unissued shares of common stock and preferred stock could render more difficult or discourage an attempt to obtain control of a majority of our common stock by means of a proxy contest, tender offer, merger or otherwise.

Exclusive Forum. Our certificate of incorporation will provide that, subject to limited exceptions, the state or federal courts located in the State of Delaware will be the sole and exclusive forum for (i) any derivative action or proceeding brought on our behalf, (ii) 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, (iii) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law, our certificate of incorporation or our bylaws, or (iv) 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 certificate of incorporation described above. Although we believe these provisions benefit us by providing increased consistency in the application of Delaware law for the specified types of actions and proceedings, the provisions may have the effect of discouraging lawsuits against our directors and officers. The enforceability of similar choice of forum provisions in other companies certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with one or more actions or proceedings described above, a court could find the choice of forum provisions contained in our certificate of incorporation to be inapplicable or unenforceable.

Section 203 of the Delaware General Corporation Law

Upon completion of this offering, we will be subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. A business combination includes, among other things, a merger, asset or stock sale or other transaction resulting in a financial benefit to the interested stockholder. An interested stockholder is a person who, together with affiliates and associates, owns, or did own within three years prior to the determination of interested stockholder status, 15% or more of the corporation s voting stock.

Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions: before the stockholder became interested, the board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder; upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 75% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some

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instances; or at or after the time the stockholder became interested, the business combination was approved by the board of directors of the corporation and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

A Delaware corporation may opt out of these provisions with an express provision in its original certificate of incorporation or an express provision in its certificate of incorporation or bylaws resulting from a stockholders amendment approved by at least a majority of the outstanding voting shares. We have not opted out of these provisions. As a result, mergers or other takeover or change in control attempts of us may be discouraged or prevented.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC.

Listing

Our common stock has been approved for listing on the NASDAQ Global Market under the symbol AKBA.

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Shares Eligible for Future Sale

Prior to this offering, there has been no public market for our common stock. Future sales of our common stock, including shares issued upon the exercise of outstanding options, in the public market after this offering, or the perception that those sales may occur, could cause the prevailing market price for our common stock to fall or impair our ability to raise equity capital at a time and price we deem appropriate. As described below, only a limited number of shares of our common stock will be available for sale in the public market for a period of several months after completion of this offering due to contractual and legal restrictions on resale described below.

Sale of Restricted Shares

Based on the number of shares of our common stock outstanding as of December 31, 2013, upon the closing of this offering and assuming (1) the conversion of our outstanding preferred stock into common stock, (2) no exercise of the underwriters option to purchase additional shares of common stock, and (3) no exercise of outstanding options, we would have had outstanding an aggregate of approximately 19,383,045 shares of common stock (including the 112,853 shares of common stock that will be issued upon conversion of the Series C preferred stock with respect to dividends accrued between December 31, 2013 and the closing of the offering, as well as ordinary course activity under the Company s equity incentive plans). Of these shares, all of the shares of common stock to be sold in this offering, and any shares sold upon exercise of the underwriters option to purchase additional shares, will be freely tradable in the public market without restriction or further registration under the Securities Act, unless the shares are held by any of our affiliates as such term is defined in Rule 144 of the Securities Act. All remaining shares of common stock held by existing stockholders immediately prior to the completion of this offering will be restricted securities as such term is defined in Rule 144. These restricted securities were issued and sold by us in private transactions and are eligible for public sale only if registered under the Securities Act or if they qualify for an exemption from registration under the Securities Act, including the exemptions provided by Rule 144 or Rule 701, which rules are summarized below.

As a result of the lock-up agreements referred to below and the provisions of Rule 144 and Rule 701 under the Securities Act, the shares of our common stock (excluding the shares sold in this offering) that will be available for sale in the public market are as follows:

Approximate Number of Shares	First Date Available for Sale into Public Market
13,500,692	180 days after the date of this prospectus upon expiration of the lock-up agreements referred to below, subject in some cases to applicable volume limitations under Rule 144

Lock-up Agreements

In connection with this offering, we, and all of our directors and officers, and the holders of substantially all of our outstanding stock and stock options have agreed that, without the prior written consent of Morgan Stanley & Co. LLC and Credit Suisse Securities (USA) LLC on behalf of the underwriters, we and they will not, during the period ending 180 days after the date of this prospectus (the restricted period):

- offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend, or otherwise transfer or dispose of, directly or indirectly, any shares of our common stock or any securities convertible into or exercisable or exchangeable for our common stock; or

enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of our common stock,

whether any such transaction described above is to be settled by delivery of common stock or such other securities, in cash or otherwise. In addition, we and all of our directors and officers, and the holders of substantially all of our common stock and stock options have agreed that, without the prior written consent of

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Morgan Stanley & Co. LLC and Credit Suisse Securities (USA) LLC on behalf of the underwriters, during the restricted period, no registration statement with the SEC relating to the offering of any shares of common stock or any security convertible into or exercisable or exchangeable for our common stock will be filed.

The restrictions described in the immediately preceding paragraph do not apply to:

the sale of shares by us to the underwriters;

the issuance by us of shares of our common stock upon the exercise of an option or warrant or the conversion of a security outstanding on the date of this prospectus of which the underwriters have been advised in writing;

the establishment of a trading plan pursuant to Rule 10b5-1 under the Exchange Act for the transfer of shares of our common stock; *provided* that such plan does not provide for the transfer of shares of our common stock during the restricted period and to the extent a public announcement or filing under the Exchange Act, if any, is required of or voluntarily made regarding the establishment of such plan, such announcement or filing shall include a statement to the effect that no transfer of common stock may be made under such plan during the restricted period;

transactions relating to shares of our common stock or other securities acquired in this offering (other than any shares of our common stock directed by us and purchased in this offering by one of our officers or directors) or in open market transactions after the date of the final prospectus;

transfers of shares of our common stock, or any security convertible into, exercisable or exchangeable for our common stock, as a bona fide gift;

transfers of shares of our common stock, or any security convertible into, exercisable or exchangeable for our common stock, by will or intestacy;

the exercise of options to purchase shares of our common stock granted under any existing stock incentive plan or stock purchase plan described in this prospectus, *provided* that any shares of our common stock issued pursuant to such exercise shall be subject to the same restrictions;

transfers to us for the purpose of satisfying tax withholding obligations upon the vesting of other equity incentive awards granted under any existing stock incentive plan or stock purchase plan described in this prospectus;

transfers or distributions not involving a disposition for value of shares of our common stock, or any security convertible into, exercisable or exchangeable for our common stock, to any limited or general partners, stockholders or members of a lock-up signatory, or if the lock-up signatory is a corporation, to a wholly-owned subsidiary of such lock-up signatory;

transfers of shares of our common stock, or any security convertible into, exercisable or exchangeable for our common stock, made by one of the lock-up signatories to (i) any trust, corporation, partnership, limited liability company or other legal entity who, directly or indirectly, controls, is controlled by, or is under common control with such lock-up signatory, (ii) any trust or other legal entity for which a lock-up signatory or the spouse of a lock-up signatory serves as trustee or investment advisor, or (iii) any member of the immediate family of a lock-up signatory, or any trust or other legal entity for the direct or indirect benefit of a lock-up signatory or any member of the immediate family of a lock-up signatory;

transfers of shares of our common stock, or any securities convertible into, exercisable or exchangeable for our common stock, pursuant to a sale of, or an offer to purchase, 100% of our outstanding common stock, whether pursuant to a merger, tender offer or otherwise, to a third party or group of third parties, *provided* that in the event that such tender offer, merger, or transaction is not completed, our common stock and any security convertible into or exchangeable for our common stock shall remain subject to the same restrictions; or

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the conversion of our outstanding preferred stock into shares of our common stock upon the closing of this offering, *provided* that such shares of our common stock shall remain subject to the same restrictions,

provided, however, that in the case of any transfer or distribution pursuant to the fifth, sixth, ninth or tenth clauses above, each donee, distributee or transferee shall sign and deliver a lock-up agreement substantially in the form of the lock-up agreements described above; and in the case of any transaction, transfer, exercise or distribution pursuant to the fourth through (and including) the tenth clauses above, no filing under Section 16(a) of the Exchange Act, reporting a reduction in beneficial ownership of shares of our common stock, shall be required or shall be voluntarily made during the restricted period (other than a filing on Form 5 made after the expiration of the restricted period).

Following the lock-up periods set forth in the agreements described above, all of the shares of our common stock that are restricted securities or are held by our affiliates as of the date of this prospectus will be eligible for sale in the public market in compliance with Rule 144 under the Securities Act.

In addition to the restrictions contained in the lock-up agreements described above, we have entered into agreements with certain of our security holders, including our amended and restated investors rights agreement and the standard forms of our option agreements under our equity incentive plans, that contain market stand-off provisions imposing restrictions on the ability of such security holders to offer, sell or transfer our equity securities for a period of 180 days following the date of this prospectus.

Rule 144

Affiliate Resales of Restricted Securities

In general, beginning 90 days after the effective date of the registration statement of which this prospectus is a part, a person who is an affiliate of ours, or who was an affiliate at any time during the 90 days before a sale, who has beneficially owned shares of our common stock for at least six months would be entitled to sell in broker s transactions or certain riskless principal transactions or to market makers, a number of shares within any three-month period that does not exceed the greater of:

1% of the number of shares of our common stock then outstanding, which will equal approximately 193,830 shares immediately after this offering; or

the average weekly trading volume in our common stock on the NASDAQ Global Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to such sale.

Affiliate resales under Rule 144 are also subject to the availability of current public information about us. In addition, if the number of shares being sold under Rule 144 by an affiliate during any three-month period exceeds 5,000 shares or has an aggregate sale price in excess of $50,000, the seller must file a notice on Form 144 with the Securities and Exchange Commission and NASDAQ concurrently with either the placing of a sale order with the broker or the execution directly with a market maker.

Non-Affiliate Resales of Restricted Securities

In general, beginning 90 days after the effective date of the registration statement of which this prospectus is a part, a person who is not an affiliate of ours at the time of sale, and has not been an affiliate at any time during the 90 days preceding a sale, and who has beneficially owned shares of our common stock for at least six months but less than a year, is entitled to sell such shares subject only to the availability of current public information about us. If such person has held our shares for at least one year, such person can resell under Rule 144(b)(1) without regard to any Rule 144 restrictions, including the 90-day public company requirement and the current public information requirement.

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Non-affiliate resales are not subject to the manner of sale, volume limitation or notice filing provisions of Rule 144.

Rule 701

In general, under Rule 701, any of an issuer s employees, directors, officers, consultants or advisors who purchases shares from the issuer in connection with a qualified compensatory stock or option plan or other written agreement before the effective date of a registration statement under the Securities Act is entitled to sell such shares 90 days after such effective date in reliance on Rule 144. An affiliate of the issuer can resell shares in reliance on Rule 144 without having to comply with the holding period requirement, and non-affiliates of the issuer can resell shares in reliance on Rule 144 without having to comply with the current public information and holding period requirements.

The Securities and Exchange Commission has indicated that Rule 701 will apply to stock options granted by an issuer before it becomes subject to the reporting requirements of the Exchange Act, along with the shares acquired upon exercise of such options, including exercises after an issuer becomes subject to the reporting requirements of the Exchange Act.

Registration Rights

Upon the completion of this offering, the holders of 13,171,517 shares of our common stock issued or issuable will be entitled to specified rights with respect to the registration of the offer and sale of their shares under the Securities Act. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act immediately upon the effectiveness of the registration statement. See the section of this prospectus titled Description of Capital Stock Registration Rights for additional information.

Equity Incentive Plans

We intend to file with the SEC a registration statement on Form S-8 under the Securities Act covering the shares of common stock that we may issue upon exercise of outstanding options or options or other equity awards to be issued under our Amended and Restated 2008 Equity Incentive Plan and 2014 Incentive Plan. Such registration statement is expected to be filed and become effective as soon as practicable after the completion of this offering. Accordingly, shares registered under such registration statement will be available for sale in the open market following its effective date, subject to Rule 144 restrictions on affiliates and the lock-up agreements described above, if applicable.

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Material United States Federal Income Tax

Considerations for Non-U.S. Holders

The following is a summary of the material U.S. federal income and estate tax considerations relating to the purchase, ownership and disposition of our common stock by Non-U.S. Holders (defined below). This summary does not purport to be a complete analysis of all the potential tax considerations relevant to Non-U.S. Holders of our common stock. This summary is based upon the Code, the Treasury regulations promulgated or proposed thereunder and administrative and judicial interpretations thereof, all as of the date hereof and all of which are subject to differing interpretations and to change at any time, possibly on a retroactive basis.

This summary assumes that shares of our common stock are held as capital assets within the meaning of Section 1221 of the Code (generally, property held for investment). This summary does not purport to deal with all aspects of U.S. federal income and estate taxation that might be relevant to particular Non-U.S. Holders in light of their particular investment circumstances or status, nor does it address specific tax considerations that may be relevant to particular persons (including, for example, financial institutions, broker-dealers, insurance companies, partnerships or other pass-through entities, certain U.S. expatriates, tax-exempt organizations, pension plans, controlled foreign corporations , passive foreign investment companies , corporations that accumulate earnings to avoid U.S. federal income tax, persons in special situations, such as those who have elected to mark securities to market or those who hold common stock as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment, or holders subject to the alternative minimum tax or the 3.8% Medicare tax on net investment income). In addition, except as explicitly addressed herein with respect to estate tax, this summary does not address estate and gift tax considerations or considerations under the tax laws of any state, local or non-U.S. jurisdiction.

For purposes of this summary, a Non-U.S. Holder means a beneficial owner of common stock that for U.S. federal income tax purposes is not an entity treated as a partnership and is not:

- an individual who is a citizen or resident of the United States;
- a corporation or any other organization taxable as a corporation for U.S. federal income tax purposes, created or organized in or under the laws of the United States, any state thereof or the District of Columbia;
- an estate, the income of which is included in gross income for U.S. federal income tax purposes regardless of its source; or
- a trust if (1) a U.S. court is able to exercise primary supervision over the trust s administration and one or more U.S. persons have the authority to control all of the trust s substantial decisions or (2) the trust has a valid election in effect under applicable Treasury regulations to be treated as a U.S. person.

If an entity that is treated as a partnership for U.S. federal income tax purposes holds our common stock, the tax treatment of persons treated as its partners for U.S. federal income tax purposes will generally depend upon the status of the partner and the activities of the partnership. Entities that are treated as partnerships for U.S. federal income tax purposes and persons holding our common stock through an entity treated as a partnership for U.S. federal income tax purposes are urged to consult their own tax advisors.

There can be no assurance that the Internal Revenue Service (IRS) will not challenge one or more of the tax consequences described herein, and we have not obtained, nor do we intend to obtain a ruling from the IRS with respect to the U.S. federal income or estate tax consequences to a

Non-U.S. Holder of the purchase, ownership or disposition of our common stock.

THIS SUMMARY IS NOT INTENDED TO BE TAX ADVICE. NON-U.S. HOLDERS ARE URGED TO CONSULT THEIR TAX ADVISORS CONCERNING THE U.S. FEDERAL INCOME AND ESTATE TAXATION, STATE, LOCAL AND NON-U.S. TAXATION AND OTHER TAX CONSEQUENCES TO THEM OF THE PURCHASE, OWNERSHIP AND DISPOSITION OF OUR COMMON STOCK.

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Distributions on Our Common Stock

As discussed under Dividend Policy above, we do not anticipate paying any cash dividends in the foreseeable future. In the event that we do make a distribution of cash or property (other than certain stock distributions) with respect to our common stock (or in the case of certain redemptions that are treated as distributions with respect to our common stock), any such distributions generally will constitute dividends for U.S. federal income tax purposes to the extent of our current and accumulated earnings and profits, if any, as determined under U.S. federal income tax principles. If a distribution exceeds our current and accumulated earnings and profits, the excess will constitute a return of capital and will first reduce the holder s adjusted tax basis in our common stock, but not below zero. Any remaining excess will be treated as capital gain, subject to the tax treatment described below in Gain on Sale, Exchange or Other Taxable Disposition of Our Common Stock . Any such distribution would also be subject to the discussion below under the sections titled Additional Withholding and Reporting Requirements and Backup Withholding and Information Reporting.

Dividends paid to a Non-U.S. Holder generally will be subject to a 30% U.S. federal withholding tax unless such Non-U.S. Holder provides us or another applicable withholding agent, as the case may be, with the appropriate IRS Form W-8, such as:

- IRS Form W-8BEN (or successor form) certifying, under penalties of perjury, that such holder is not a United States person (as defined under the Code) and is eligible for a reduction in the rate of, or exemption from, withholding under an applicable income tax treaty, or

- IRS Form W-8ECI (or successor form) certifying that a dividend paid on common stock is not subject to withholding tax because it is effectively connected with a trade or business in the United States of the Non-U.S. Holder (in which case such dividend generally will be subject to regular graduated U.S. tax rates as described below).

The certification requirement described above must be provided to us or another applicable withholding agent prior to the payment of dividends and must be updated periodically. The certification also may require a Non-U.S. Holder that claims treaty benefits of a reduction in the rate of, or exemption from, withholding on dividends to provide its U.S. taxpayer identification number. Special certification and other requirements apply in the case of certain Non-U.S. Holders that hold shares of our common stock through intermediaries or are pass-through entities for U.S. federal income tax purposes.

Each Non-U.S. Holder is urged to consult its own tax advisor about the specific methods for satisfying these requirements. A claim for exemption will not be valid if the person receiving the applicable form has actual knowledge or reason to know that the statements on the form are false.

If dividends are effectively connected with a trade or business in the United States of a Non-U.S. Holder (and, if required by an applicable income tax treaty, attributable to a U.S. permanent establishment or fixed base), the Non-U.S. Holder, although exempt from the withholding tax described above (provided that the certifications described above are satisfied), generally will be subject to U.S. federal income tax on such dividends on a net income basis in the same manner as if it were a U.S. person. In addition, if a Non-U.S. Holder is treated as a corporation for U.S. federal income tax purposes, the Non-U.S. Holder may be subject to an additional branch profits tax equal to 30% (unless reduced by an applicable income tax treaty) of such effectively connected dividend, as adjusted for certain items.

Non-U.S. Holders that do not timely provide us or another applicable withholding agent with the required certification, but which are eligible for a reduced rate of, or an exemption from, U.S. federal withholding tax, may obtain a refund or credit of any excess amount withheld by timely

filing an appropriate claim for refund with the IRS.

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Gain on Sale, Exchange or Other Taxable Disposition of Our Common Stock

Subject to the discussion below under the sections titled Additional Withholding and Reporting Requirements and Backup Withholding and Information Reporting , in general, a Non-U.S. Holder will not be subject to U.S. federal income tax or withholding tax on gain realized upon such holder s sale, exchange or other taxable disposition of shares of our common stock unless (i) such Non-U.S. Holder is an individual who is present in the United States for 183 days or more in the taxable year of disposition, and certain other conditions are met; (ii) we are or have been a United States real property holding corporation , as defined in the Code (a USRPHC), at any time within the shorter of the five-year period preceding the disposition and the Non-U.S. Holder s holding period in the shares of our common stock, and certain other requirements are met; or (iii) such gain is effectively connected with the conduct by such Non- U.S. Holder of a trade or business in the United States (and, if required by an applicable income tax treaty, is attributable to a permanent establishment or fixed base maintained by such Non-U.S. Holder in the United States).

If the first exception applies, the Non-U.S. Holder generally will be subject to U.S. federal income tax at a rate of 30% (or at a reduced rate under an applicable income tax treaty) on the amount by which such Non-U.S. Holder s capital gains allocable to U.S. sources exceed capital losses allocable to U.S. sources during the taxable year of the disposition. If the third exception applies, the Non-U.S. Holder generally will be subject to U.S. federal income tax with respect to such gain on a net income basis in the same manner as if it were a U.S. person, and a Non-U.S. Holder that is a corporation for U.S. federal income tax purposes may also be subject to a branch profits tax with respect to such effectively connected gain, as adjusted for certain items, at a rate of 30% (or at a reduced rate under an applicable income tax treaty).

Regarding the second exception, generally, a corporation is a USRPHC only if the fair market value of its U.S. real property interests (as defined in the Code) equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. Although there can be no assurance in this regard, we believe that we are not, and do not anticipate becoming, a USRPHC. However, because the determination of whether we are a USRPHC depends on the fair market value of our U.S. real property interests relative to the fair market value of our other business assets, there can be no assurance that we have not been a USRPHC in the past and will not become a USRPHC in the future. Even if we became a USRPHC, a Non-U.S. Holder would not be subject to U.S. federal income tax on a sale, exchange or other taxable disposition of our common stock by reason of our status as USRPHC so long as our common stock is regularly traded on an established securities market (within the meaning of the applicable regulations) and such Non-U.S. Holder does not own and is not deemed to own (directly, indirectly or constructively) more than 5% of our outstanding common stock at any time during the shorter of the five year period ending on the date of disposition and such holder s holding period. However, no assurance can be provided that our common stock will be regularly traded on an established securities market for purposes of the rules described above. Prospective investors are encouraged to consult their own tax advisors regarding the possible consequences to them if we are, or were to become, a USRPHC.

Additional Withholding and Reporting Requirements

Legislation enacted in March 2010 and related guidance (commonly referred to as FATCA) will impose, in certain circumstances, U.S. federal withholding at a rate of 30% on payments of (a) dividends on our common stock on or after July 1, 2014, and (b) gross proceeds from the sale or other disposition of our common stock on or after January 1, 2017. In the case of payments made to a foreign financial institution as defined under FATCA (including, among other entities, an investment fund), the tax generally will be imposed, subject to certain exceptions, unless such institution (i) enters into (or is otherwise subject to) and complies with an agreement with the U.S. government (a FATCA Agreement) or (ii) complies with an applicable intergovernmental agreement between the United States and a foreign jurisdiction (an IGA) or any foreign law implementing an applicable IGA, in either case to, among other things, collect and provide to the U.S. or other relevant tax authorities certain information regarding U.S. account holders of such institution. In the case of

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payments made to a foreign entity that is not a foreign financial institution, the tax generally will be imposed, subject to certain exceptions, unless such foreign entity provides the withholding agent with a certification that it does not have any substantial U.S. owners (generally, any specified U.S. persons that directly or indirectly owns more than a specified percentage of such entity) or that identifies its substantial U.S. owners. If our common stock is held through a foreign financial institution that enters into (or is otherwise subject to) a FATCA Agreement, such foreign financial institution (or, in certain cases, a person paying amounts to such foreign financial institution) generally will be required, subject to certain exceptions, to apply FATCA withholding on payments of dividends and proceeds described above made to (x) a person (including an individual) that fails to comply with certain information requests or (y) a foreign financial institution that has not entered into a FATCA Agreement and is not otherwise exempt from FATCA pursuant to an IGA.

Prospective investors should consult their own tax advisors regarding the possible impact of these rules on their investment in our common stock, and the entities through which they hold our common stock, including, without limitation, the process and deadlines for meeting the applicable requirements to prevent the imposition of this 30% withholding tax under FATCA.

Backup Withholding and Information Reporting

We must report annually to the IRS and to each Non-U.S. Holder the gross amount of the distributions on our common stock paid to the holder and the tax withheld, if any, with respect to the distributions. Non-U.S. Holders may have to comply with specific certification procedures to establish that the holder is not a United States person (as defined in the Code) in order to avoid backup withholding at the applicable rate, currently 28%, with respect to dividends on our common stock. Dividends paid to Non-U.S. Holders subject to U.S. withholding, as described above under the section titled Distributions on Our Common Stock , generally will be exempt from U.S. backup withholding.

Information reporting and backup withholding will generally apply to the proceeds of a disposition of our common stock by a Non-U.S. Holder effected by or through the U.S. office of any broker, U.S. or foreign, unless the holder certifies, under penalties of perjury, that it is not a United States person (as defined under the Code) and satisfies certain other requirements (and the payor does not have actual knowledge or reason to know that the beneficial owner is a United States person), or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a Non-U.S. Holder where the transaction is effected outside the United States through a non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker. Prospective investors should consult their own tax advisors regarding the application of the information reporting and backup withholding rules to them.

Copies of information returns may be made available to the tax authorities of the country in which the Non-U.S. Holder resides or in which the Non-U.S. Holder is incorporated, under the provisions of a specific treaty or agreement.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a Non-U.S. Holder can be refunded or credited against the Non-U.S. Holder s U.S. federal income tax liability, if any, provided that an appropriate claim is timely filed with the IRS.

Federal Estate Tax

Common stock owned (or treated as owned) by an individual who is not a citizen or a resident of the United States (as defined for U.S. federal estate tax purposes) at the time of death will be included in the individual s gross estate for U.S. federal estate tax purposes unless an applicable estate or other tax treaty provides otherwise, and therefore, may be subject to U.S. federal estate tax.

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Underwriting

Subject to the terms and conditions stated in the underwriting agreement dated the date of this prospectus, the underwriters named below, for whom Morgan Stanley & Co. LLC, Credit Suisse Securities (USA) LLC and UBS Securities LLC are acting as representatives, have severally agreed to purchase, and we have agreed to sell to them, severally, the number of shares indicated below:

Name	Number of Shares
Morgan Stanley & Co. LLC	2,132,353
Credit Suisse Securities (USA) LLC	2,132,353
UBS Securities LLC	1,176,471
Nomura Securities International, Inc.	441,176
Total	5,882,353

The underwriters and the representatives are collectively referred to as the underwriters and the representatives, respectively. The underwriters are offering the shares of common stock subject to their acceptance of the shares from us and subject to prior sale. The underwriting agreement provides that the obligations of the several underwriters to pay for and accept delivery of the shares of common stock offered by this prospectus are subject to the approval of certain legal matters by their counsel and to certain other conditions. The underwriters are obligated to take and pay for all of the shares of common stock offered by this prospectus if any such shares are taken. However, the underwriters are not required to take or pay for the shares covered by the underwriters over-allotment option described below.

The underwriters initially propose to offer part of the shares of common stock directly to the public at the offering price listed on the cover page of this prospectus and part to certain dealers at a price that represents a concession not in excess of $0.71 a share under the public offering price. After the initial offering of the shares of common stock, the offering price and other selling terms may from time to time be varied by the representatives.

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase up to 879,647 additional shares of common stock at the public offering price listed on the cover page of this prospectus, less underwriting discounts and commissions. The underwriters may exercise this option solely for the purpose of covering over-allotments, if any, made in connection with the offering of the shares of common stock offered by this prospectus. To the extent the option is exercised, each underwriter will become obligated, subject to certain conditions, to purchase the same percentage of the additional shares of common stock as the number listed next to the underwriter s name in the preceding table bears to the total number of shares of common stock listed next to the names of all underwriters in the preceding table.

The following table shows the per share and total public offering price, underwriting discounts and commissions, and proceeds before expenses to us. These amounts are shown assuming both no exercise and full exercise of the underwriters option to purchase up to an additional 879,647 shares of common stock.

	Per Share	Total	
		No exercise	Full exercise
Public Offering Price	$ 17.00	$ 100,000,001	$ 114,954,000
Underwriting Discount and commissions to be paid by us	$ 1.19	$ 7,000,000	$ 8,046,780

Proceeds, before expenses, to us	$ 15.81	$ 93,000,001	$ 106,907,220

The estimated offering expenses payable by us, exclusive of the underwriting discounts and commissions, are approximately $2.8 million. We have agreed to reimburse the underwriters for expenses relating to clearance of

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this offering with the Financial Industry Regulatory Authority, Inc. and the qualification of our common stock under state securities laws (in an amount not to exceed in the aggregate $50,000).

The underwriters have informed us that they do not intend sales to discretionary accounts to exceed 5% of the total number of shares of common stock offered by them.

Our common stock has been approved for listing on the Nasdaq Global Market under the trading symbol AKBA.

We, and all of our directors and officers, and the holders of substantially all of our outstanding stock and stock options have agreed that, without the prior written consent of Morgan Stanley & Co. LLC and Credit Suisse Securities (USA) LLC on behalf of the underwriters, we and they will not, during the period ending 180 days after the date of this prospectus (the restricted period):

- offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend, or otherwise transfer or dispose of, directly or indirectly, any shares of our common stock or any securities convertible into or exercisable or exchangeable for our common stock; or

- enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of our common stock,

whether any such transaction described above is to be settled by delivery of common stock or such other securities, in cash or otherwise. In addition, we and all of our directors and officers, and the holders of substantially all of our common stock and stock options have agreed that, without the prior written consent of Morgan Stanley & Co. LLC and Credit Suisse Securities (USA) LLC on behalf of the underwriters, during the restricted period, no registration statement with the SEC relating to the offering of any shares of common stock or any security convertible into or exercisable or exchangeable for common stock will be filed.

The restrictions described in the immediately preceding paragraph to do not apply to:

- the sale of shares by us to the underwriters;

- the issuance by us of shares of our common stock upon the exercise of an option or warrant or the conversion of a security outstanding on the date of this prospectus of which the Underwriters have been advised in writing;

- the establishment of a trading plan pursuant to Rule 10b5-1 under the Exchange Act for the transfer of shares of our common stock; *provided* that such plan does not provide for the transfer of shares of our common stock during the restricted period and to the extent a public announcement or filing under the Exchange Act, if any, is required of or voluntarily made regarding the establishment of such plan, such announcement or filing shall include a statement to the effect that no transfer of common stock may be made under such plan during the restricted period;

transactions relating to shares of our common stock or other securities acquired in this offering (other than any shares of our common stock directed by us and purchased in this offering by one of our officers or directors) or in open market transactions after the date of the final prospectus;

transfers of shares of our common stock, or any security convertible into, exercisable or exchangeable for our common stock, as a bona fide gift;

transfers of shares of our common stock, or any security convertible into, exercisable or exchangeable for our common stock, by will or intestacy;

the exercise of options to purchase shares of our common stock granted under any existing stock incentive plan or stock purchase plan described in this prospectus, *provided* that any shares of our common stock issued pursuant to such exercise shall be subject to the same restrictions;

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transfers to us for the purpose of satisfying tax withholding obligations upon the vesting of other equity incentive awards granted under any existing stock incentive plan or stock purchase plan described in this prospectus;

transfers or distributions not involving a disposition for value of shares of our common stock, or any security convertible into, exercisable or exchangeable for our common stock, to any limited or general partners, stockholders or members of a lock-up signatory, or if the lock-up signatory is a corporation, to a wholly-owned subsidiary of such lock-up signatory;

transfers of shares of our common stock, or any security convertible into, exercisable or exchangeable for our common stock, made by one of the lock-up signatories to (i) any trust, corporation, partnership, limited liability company or other legal entity who, directly or indirectly, controls, is controlled by, or is under common control with such lock-up signatory, (ii) any trust or other legal entity for which a lock-up signatory or the spouse of a lock-up signatory serves as trustee or investment advisor, or (iii) any member of the immediate family of a lock-up signatory, or any trust or other legal entity for the direct or indirect benefit of a lock-up signatory or any member of the immediate family of a lock-up signatory;

transfers of shares of our common stock, or any securities convertible into, exercisable or exchangeable for our common stock, pursuant to a sale of, or an offer to purchase, 100% of our outstanding common stock, whether pursuant to a merger, tender offer or otherwise, to a third party or group of third parties, *provided* that in the event that such tender offer, merger, or transaction is not completed, our common stock and any security convertible into or exchangeable for our common stock shall remain subject to the same restrictions; or

the conversion of our outstanding preferred stock into shares of our common stock upon the closing of this offering, *provided* that such shares of our common stock shall remain subject to the same restrictions,

provided, *however*, that in the case of any transfer or distribution pursuant to the fifth, sixth, ninth or tenth clauses above, each donee, distributee or transferee shall sign and deliver a lock-up agreement substantially in the form of the lock-up agreements described above; and in the case of any transaction, transfer, exercise or distribution pursuant to the fourth through (and including) the tenth clauses above, no filing under Section 16(a) of the Exchange Act, reporting a reduction in beneficial ownership of shares of our common stock, shall be required or shall be voluntarily made during the restricted period (other than a filing on Form 5 made after the expiration of the restricted period).

Morgan Stanley & Co. LLC and Credit Suisse Securities (USA) LLC, in their sole discretion, may release the common stock and other securities subject to the lock-up agreements described above in whole or in part at any time.

In order to facilitate the offering of the common stock, the underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the common stock. Specifically, the underwriters may sell more shares than they are obligated to purchase under the underwriting agreement, creating a short position. A short sale is covered if the short position is no greater than the number of shares available for purchase by the underwriters under the over-allotment option. The underwriters can close out a covered short sale by exercising the over-allotment option or purchasing shares in the open market. In determining the source of shares to close out a covered short sale, the underwriters will consider, among other things, the open market price of shares compared to the price available under the over-allotment option. The underwriters may also sell shares in excess of the over-allotment option, creating a naked short position. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchase in this offering. As an additional means of facilitating this offering, the underwriters may bid for, and purchase, shares of common stock in the open market to stabilize

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the price of the common stock. These activities may raise or maintain the market price of the common stock above independent market levels or prevent or retard a decline in the market price of the common stock. The underwriters are not required to engage in these activities and may end any of these activities at any time.

We and the underwriters have agreed to indemnify each other against certain liabilities, including liabilities under the Securities Act.

A prospectus in electronic format may be made available on websites maintained by one or more underwriters, or selling group members, if any, participating in this offering. The representatives may agree to allocate a number of shares of common stock to underwriters for sale to their online brokerage account holders. Internet distributions will be allocated by the representatives to underwriters that may make Internet distributions on the same basis as other allocations.

Other Relationships

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, principal investment, hedging, financing and brokerage activities. Certain of the underwriters and their respective affiliates have, from time to time, performed, and may in the future perform, various financial advisory and investment banking services for us, for which they received or will receive customary fees and expenses.

In addition, in the ordinary course of their various business activities, the underwriters and their respective affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers and may at any time hold long and short positions in such securities and instruments. Such investment and securities activities may involve our securities and instruments. The underwriters and their respective affiliates may also make investment recommendations or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long or short positions in such securities and instruments.

Pricing of the Offering

Prior to this offering, there has been no public market for our common stock. The initial public offering price was determined by negotiations between us and the representatives. Among the factors considered in determining the initial public offering price were our future prospects and those of our industry in general, financial and operating information in recent periods, and the price-earnings ratios, price-sales ratios, market prices of securities and certain financial and operating information of companies engaged in activities similar to ours.

Directed Share Program

At our request, the underwriters have reserved 162,000 shares of common stock to be issued by us and offered by this prospectus for sale, at the initial public offering price, to directors, officers, employees, business associates and related persons of Akebia Therapeutics, Inc. The number of shares of common stock available for sale to the general public will be reduced to the extent these individuals purchase such reserved shares.

Any reserved shares that are not so purchased will be offered by the underwriters to the general public on the same basis as the other shares offered by this prospectus.

Selling Restrictions

European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a Relevant Member State) an offer to the public of any shares of our common stock may not

be made in that Relevant Member State, except that an offer to the public in that Relevant Member State of any shares of our common stock may be made at any time under the following exemptions under the Prospectus Directive, if they have been implemented in that Relevant Member State:

(a) to any legal entity which is a qualified investor as defined in the Prospectus Directive;

(b) to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representatives for any such offer; or

(c) in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of shares of our common stock shall result in a requirement for the publication by us or any underwriter of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an offer to the public in relation to any shares of our common stock in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and any shares of our common stock to be offered so as to enable an investor to decide to purchase any shares of our common stock, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State, the expression Prospectus Directive means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State), and includes any relevant implementing measure in the Relevant Member State, and the expression 2010 PD Amending Directive means Directive 2010/73/EU.

United Kingdom

Each underwriter has represented and agreed that:

(a) it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the Financial Services and Markets Act 200 (FSMA)) received by it in connection with the issue or sale of the shares of our common stock in circumstances in which Section 21(1) of the FSMA does not apply to us; and

(b) it has complied and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to the shares of our common stock in, from or otherwise involving the United Kingdom.

Switzerland

The Prospectus does not constitute an issue prospectus pursuant to Article 652a or Article 1156 of the Swiss Code of Obligations (CO) and the shares will not be listed on the SIX Swiss Exchange. Therefore, the Prospectus may not comply with the disclosure standards of the CO and/or the listing rules (including any prospectus schemes) of the SIX Swiss Exchange. Accordingly, the shares may not be offered to the public in or from Switzerland, but only to a selected and limited circle of investors, which do not subscribe to the shares with a view to distribution.

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Legal Matters

The validity of the common stock offered in this prospectus will be passed upon for us by Ropes & Gray LLP, Boston, Massachusetts. Certain legal matters in connection with this offering will be passed upon for the underwriters by Latham & Watkins LLP, Boston, Massachusetts.

Experts

The financial statements of Akebia Therapeutics, Inc. (a development stage company) at December 31, 2013 and 2012, and for each of the two years in the period ended December 31, 2013, and for the period February 27, 2007 (inception) through December 31, 2013, appearing in this Prospectus and Registration Statement have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon appearing elsewhere herein, and are included in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

Where You Can Find More Information

We have filed with the SEC a registration statement on Form S-1 under the Securities Act with respect to the shares of common stock offered hereby. This prospectus, which constitutes a part of the registration statement, does not contain all of the information set forth in the registration statement or the exhibits and schedules filed therewith. For further information with respect to us and the common stock offered hereby, reference is made to the registration statement and the exhibits and schedules filed therewith. Statements contained in this prospectus regarding the contents of any contract or any other document that is filed as an exhibit to the registration statement are not necessarily complete, and each such statement is qualified in all respects by reference to the full text of such contract or other document filed as an exhibit to the registration statement. A copy of the registration statement and the exhibits and schedules filed therewith may be inspected without charge at the public reference room maintained by the SEC, located at 100 F Street N.E., Washington, D.C. 20549, and copies of all or any part of the registration statement may be obtained from such offices upon the payment of the fees prescribed by the SEC. Please call the SEC at 1-800-SEC-0330 for further information about the public reference room. The SEC also maintains a website that contains reports, proxy and information statements and other information regarding registrants that file electronically with the SEC. The address is www.sec.gov.

Upon completion of this offering, we will become subject to the information and periodic reporting requirements of the Exchange Act and, in accordance therewith, will file periodic reports, proxy statements and other information with the SEC. Such periodic reports, proxy statements and other information will be available for inspection and copying at the public reference room and website of the SEC referred to above.

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Akebia Therapeutics, Inc.

(A Development Stage Company)

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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 balance sheets of Akebia Therapeutics, Inc. (a development stage company) as of December 31, 2013 and 2012, and the related statements of operations and comprehensive loss, redeemable convertible preferred stock and stockholders equity (deficit) and cash flows for each of the two years in the period ended December 31, 2013, and for the period from February 27, 2007 (inception) through December 31, 2013. 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 financial position of Akebia Therapeutics, Inc. (a development stage company) at December 31, 2013 and 2012, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2013 and for the period from February 27, 2007 (inception) through December 31, 2013, in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP

Cincinnati, Ohio

February 14, 2014,

except as it relates to Note 16

as to which the date is March 7, 2014

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Akebia Therapeutics, Inc.

(A Development Stage Company)

Balance Sheets

	December 31, 2012	December 31, 2013 Actual	December 31, 2013 Pro forma (unaudited)
Assets			
Current assets:			
Cash and cash equivalents	$ 1,641,038	$ 21,215,228	$ 21,215,228
Investments		11,341,241	11,341,241
Accounts receivable	85,633	135,339	135,339
Prepaid expenses and other current assets	517,202	739,235	739,235
Total current assets	2,243,873	33,431,043	33,431,043
Equipment, net of accumulated depreciation of $1,282 at December 31, 2013		30,366	30,366
Deferred offering costs		1,078,138	1,078,138
Other assets		125,345	125,345
Total assets	$ 2,243,873	$ 34,664,892	$ 34,664,892
Liabilities, redeemable convertible preferred stock and stockholders deficit			
Current liabilities:			
Accounts payable	$ 417,943	$ 714,137	$ 714,137
Accrued expenses	351,250	3,183,761	3,183,761